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175. *Magnetochemistry. Part III.* Compounds of Bivalent Copper.*

By B. N. Figgis and C. M. Harris.

The temperature dependence of the magnetic susceptibility of 9 cupric co-ordination compounds is reported over the temperature range 80—300° K. The significance of the results is discussed with regard to stereochemistry and bond type in cupric complexes. It is found that the magnetic moments of 1·8—2·0 B.M. at room temperature are essentially independent of temperature.

There have been many measurements of the magnetic properties of bivalent copper compounds, mostly at room temperature only. It seems well established that, under conditions of adequate magnetic dilution the cupric ion exhibits a moment somewhat above the spin-only value for the one unpaired electron configuration of d^9, *i.e.*, 1·73 B.M. This is as expected for the cupric ion, at least if the ligand distribution around it is essentially octahedral. However, a number of points need clarification, particularly in regard to the stereochemistry and bonding of the cupric ion.

Ray and Sen [1] reported the moments at room temperature and, in some instances, at unspecified lower temperatures, of a number of typical cupric co-ordination complexes. They correlate the magnetic moments of 1·7—1·9 B.M. on the one hand with a red-yellow colour, and of 1·9—2·2 B.M. on the other with a green-blue colour. They attribute to the latter group a tetrahedral stereochemistry of the attached ligands on the grounds that such an arrangement might well lead to higher moments than does the octahedral arrangement of the ligands which they assigned to the former group. The larger moments reported by Ray and Sen were often associated with very high values of θ, the Weiss constant in the Curie–Weiss law, of up to 100°. The moments they found were calculated by means of the expression $\mu'_{eff} = 2{\cdot}84\sqrt{[\chi_{Cu}(T + \theta)]}$. When calculated as $\mu_{eff} = 2{\cdot}84\sqrt{(\chi_{Cu}T)}$, moments higher than 2·0 B.M. are not observed at room temperature. In no case, other than for some distorted octahedral arrangements, was the stereochemistry certain. These high values of θ are at variance with the other available data on cupric compounds, and are difficult to understand when they occur in complexes of octahedral stereochemistry. We have repeated the measurements of the susceptibility over a range of temperature for two of the compounds concerned, Cu(dimethylglyoxime)Cl_2 and Cu(glycine)$_2$,H_2O, and find very small values of θ in place of ~100°. It may be that such high values of θ are due to the lack of magnetic dilution, as in the acetate [2] and formate [3] of copper, but this is unlikely and would invalidate all but the most careful arguments based on the moments to which they pertain.

As shown in Fig. 1, the Cu^{2+} ion gives rise to a ^2D spectroscopic state which is split by an octahedral crystalline field into an upper orbital triplet (d_ϵ) and a lower lying "non-magnetic" doublet (d_γ). The separation is ~10,000—20,000 cm.$^{-1}$. The term "non-magnetic" has been used [4] to emphasise the fact that these levels cannot by themselves form part of the orbital contribution to the moment in spite of their orbital degeneracy; it does not apply to the spin contribution to the moment which these levels may make. The green-blue colours frequently observed for cupric complexes can be attributed to transitions between the d_γ–d_ϵ ligand field levels, and have values of $\epsilon_{max.}$ (extinction coefficient) of 10—100 consistent with this. The red, deeper-coloured complexes, on the

* Parts I and II, *J.*, 1959, 331, 338.

[1] Ray and Sen, *J. Indian Chem. Soc.*, 1948, **25**, 473.
[2] Figgis and Martin, *J.*, 1956, 3837.
[3] Martin and Whitley, *J.*, 1958, 1394.
[4] Bethe, *Z. Physik*, 1930, **60**, 218.

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other hand, appear to owe their colour to charge-transfer bands of $\varepsilon_{max.} \geqslant 1000$ at energies $\geqslant 20{,}000$ cm.$^{-1}$, *e.g.*, the $[CuCl_3]^-$ ion in nitrobenzene.[5]

In a tetrahedral complex the d_ϵ levels lie lowest. Although the d_γ levels cannot give rise to orbital contribution, there is, as Polder[6] has shown, a considerable interaction between the d_γ and d_ϵ levels by means of the fairly large spin–orbit coupling constant of the Cu^{2+} ion ($A = 852$ cm.$^{-1}$). This effect gives rise to the quite appreciable orbital contribution observed in the moment of, say, $CuSO_4,5H_2O$ (1·95 B.M.). A tetragonal ligand field is usually present in addition to the main one of cubic symmetry in " octahedral " cupric complexes; it arises from a lifting of the degeneracy of the d_γ^3 ground state by means of the Jahn–Teller effect with a consequent distortion of the octahedral ligand arrangement of small magnitude.[7] Polder invoked an improbably large tetragonal field distortion, a splitting of the d_γ levels of ~10,000 cm.$^{-1}$, and considered only the case when the $d_{x^2-y^2}$ orbital contained the unpaired electron. However, Polder's explanation of the orbital contribution is independent of the magnitude of the tetragonal splitting or

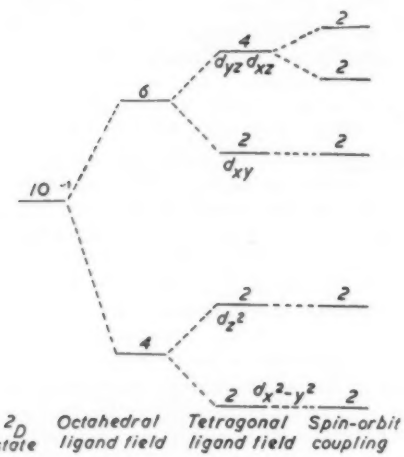

FIG. 1. *Splitting of the ^2D state of the cupric ion. The numbers above a level indicate the degeneracy to a magnetic field. The splitting by a tetragonal field component corresponds to the elongation of an octahedron in the z axis; it is reversed for a tetragonal component of the opposite sign.*

its sign provided that only the mean susceptibility, as distinct from the magnetic anisotropy, is considered. Whichever of the $d_{x^2-y^2}$ or d_{z^2} orbitals lies lowest, the moment is given by the spin-only value of 1·73 B.M. multiplied by the factor $(1 + 2A/\Delta)$, where Δ is the d_ϵ–d_γ separation. With Δ ~20,000 cm.$^{-1}$ a moment of about 1·88 B.M. is predicted for an octahedral complex. Since the d_γ levels are " non-magnetic " the ground level in an octahedral complex must be a spin (Kramer's) doublet or, if the d_γ levels are degenerate within kT, a mixture of two spin doublets of identical mean magnetic properties. Consequently, the magnetic susceptibilities of octahedral cupric complexes should follow the Curie law closely, as there is no mechanism for ground-state levels of different magnetic properties separated by ~kT. This prediction is in keeping with most of the data on the magnetic behaviour of the cupric ion.

When the stereochemistry of the ligand distribution around the cupric ion ceases to be even approximately octahedral it is no longer possible to make accurate predictions about the magnetic properties of the ion in most cases. The extension of the tetragonal distortion of the octahedral case to the complete removal of one or two *trans*-ligands to leave a tetragonal pyramidal or a square planar complex is expected to change the magnetic

[5] Nyholm, *J.*, 1951, 1767.
[6] Polder, *Physica*, 1942, **9**, 709.
[7] Dunitz and Orgel, *Nature*, 1957, **179**, 462.

properties comparatively little from those of octahedral complexes. The significance of Δ in the expression $\mu = \mu_{\text{spin-only}}(1 + 2A/\Delta)$ is then the separation between the $d_{x^2-y^2}$ and the d_{xz} and d_{yz} orbitals, as illustrated in Fig. 1 of Part II of this series.[8] When the stereochemistry is tetrahedral it might be expected, as suggested by Ray and Sen, that the ground state of the ion would be more complicated and lead to higher moments and more complicated magnetic behaviour than in the octahedral case. If there is no ligand field of lower than tetrahedral symmetry the magnetic behaviour should be similar to that of the octahedral d_ϵ^5 configuration, as set out by Kotani.[9,10] For Cu^{2+}, kT/A is about 0·25 at room temperature, and moments of about 2·2 B.M., together with some small departure from the Curie law, are predicted. However, it is likely that the degeneracy of the ground state in this case also would be lifted by a Jahn–Teller mechanism and this, in the form of a ligand field of lower symmetry, could lead to modified magnetic behaviour.

In order to try to clarify the position we have measured the susceptibilities of a number of cupric complexes of various types of stereochemistry over the temperature range 80—300° K. It was not possible to test in a satisfactory manner the considerations on the tetrahedral configuration, for there is only one compound available which is known with certainty to have even approximately that stereochemistry, *i.e.*, Cs_2CuCl_4, and it is not possible to generalise too far from a single example.

Discussion.—The results of the measurements which we have performed on the magnetic properties of cupric complexes are set out in the Table and Figs. 2—4. It is not certain in every case what the stereochemistry of the ligand distribution around the cupric ion is, for *X*-ray information on the structure is available in only some instances. However, the cases where this information is lacking are those where there seems to be no reason to doubt an octahedral or distorted octahedral arrangement. The striking feature of the results is that the moments all lie within the range 1·7—2·0 B.M. over the entire temperature range, and that the values of the Weiss constant, θ, are uniformly small—in no case above 9°.

Diamagnetic corrections, magnetic moments at 300° *and* 90° K, θ *values and accuracies of the measurements of relative susceptibilities at different temperatures for the compounds of bivalent copper studied.*

Compound	Colour	Diamagnetic corrn./ mole, $\times 10^6$	$\mu_{\text{eff.}}$ 90° K (B.M.)	$\mu_{\text{eff.}}$ 300° K (B.M.)	θ	Accuracy (%)
Cu(*o*-phenanthroline)$_3$(ClO$_4$)$_2$ ...	Pale blue	395	1·96	1·91	−9°	1
Cu(dipyridyl)$_3$(ClO$_4$)$_2$	Blue	380	1·91	1·96	5	1
$CsCuCl_3$	Garnet	105	1·93	1·95	1	1
Cu(*o*-phenanthroline)$_2$Br(ClO$_4$)...	Green-blue	280	1·68	1·72	8	0·5
Cu(*o*-phenanthroline)$_2$Br$_2$	Pale green	285	1·74	1·75	5	1
Cu(acetylacetone)$_2$	Blue	120	1·89	1·90	0	2
Cu(dimethylglyoxime)Cl$_2$	Deep green	170	1·84	1·85	4	2
Cu(*o*-phenanthroline)$_2$(ClO$_4$)$_2$ ...	Green-blue	275	1·94	1·89	−7	1
Cs_2CuCl_4	Brown-yellow	165	1·99	2·00	1	1

The case of octahedral or almost octahedral symmetry has been the subject of most studies in the literature where the stereochemistry has been known for certain. The temperature dependence of the susceptibilities of numerous Tutton salts, where the ligand field is known to be cubic with a small trigonal component, have been reported;[11-13] θ is invariably small. Of the compounds reported in this work there seems to be no reason to doubt the octahedral stereochemistry of Cu(*o*-phenanthroline)$_3$(ClO$_4$)$_2$ and Cu(dipyridyl)$_3$(ClO$_4$)$_2$, particularly as the former is isomorphous with the nickel

[8] Figgis and Nyholm, *J.*, 1959, 338.
[9] Kotani, *J. Phys. Soc. Japan*, 1949, **94**, 293.
[10] Cf. Earnshaw, Figgis, Lewis, and Nyholm, *Nature*, 1957, **179**, 1121.
[11] Krishnan and Mookherji, *Phil. Trans.*, 1938, *A*, **238**, 125.
[12] Hupse, *Physica*, 1942, **9**, 633.
[13] Bose, Datta, and Mitra, *Proc. Roy. Soc.*, 1957, *A*, **239**, 165.

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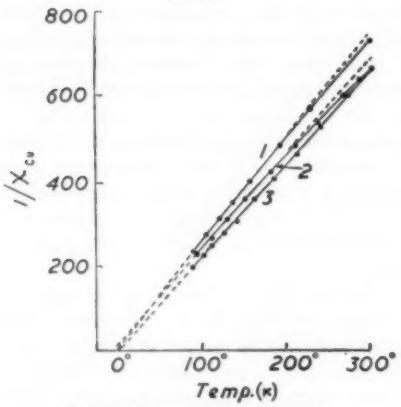
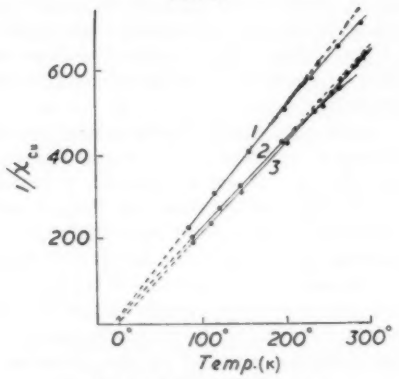
derivative.[14] The environment of the Cu^{2+} ion in $CsCuCl_3$ is known to be approximately octahedral from the *X*-ray structure determination.[15] Taken in conjunction with the well-established $\theta = 1°$ for $CuSO_4,5H_2O$ (see Part I [16]), it seems certain that the magnetic behaviour of the ground state of the cupric ion in an octahedral environment is very simple, in accord with the theory outlined above. The moments, at about 1·9 B.M., are close to those reported in refs. 11—13, and are in accord with the theory.

FIG. 2.



1, Cu(*o*-phenanthroline)$_3$(ClO$_4$)$_2$.
2, Cu(dimethylglyoxime)Cl$_2$.
3, Cu(acetylacetone)$_2$.

FIG. 3.



1, Cu(*o*-phenanthroline)$_3$Br$_2$.
2, Cu(dipyridyl)$_3$(ClO$_4$)$_2$.
3, CsCuCl$_3$.

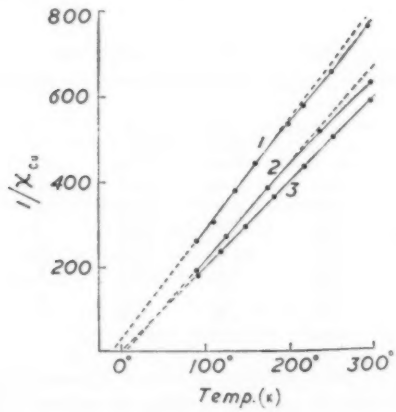


FIG. 4.

1, Cu(*o*-phenanthroline)$_2$Br(ClO$_4$)
2, Cu(*o*-phenanthroline)$_3$(ClO$_4$)$_2$.
3, Cs_2CuCl_4.

A stereochemistry of a distorted octahedral form is probably to be assigned to the compounds Cu(*o*-phenanthroline)$_2$Br$_2$ and Cu(*o*-phenanthroline)$_2$Br(ClO$_4$). Although the behaviour of the magnetic properties of these complexes with temperature is simple, with θ small, they show a moment a good deal lower than that for the other cupric complexes reported here and in the literature (apart from Ray and Sen), at 1·7 B.M. No obvious reason for such a low value of the moment in a cupric complex is apparent from the theory;

[14] Harris and Stevenson, unpublished work.
[15] Wells, *J.*, 1947, 1662.
[16] Figgis and Nyholm, *J.*, 1959, 331.

however, in the absence of evidence as to the actual stereochemistry it is not known whether any significance is to be attached to the result. To this information may be added the result [17] of $\mu_{eff} = 1{\cdot}9$ B.M. and $\theta = 0°$ for $Cu(glycine)_2,H_2O$.

The stereochemistry of the cupric ion in $Cu(acetylacetone)_2$ is known to be square planar from *X*-ray data.[18] Similarly, the nitrogen and chlorine atoms in Cu(dimethylglyoxime)Cl_2 are known to be coplanar. In the absence of *X*-ray information it seems reasonable to assign the square planar stereochemistry to $Cu(o\text{-phenanthroline})_2(ClO_4)_2$. Once again the moments are found to be about 1·9 B.M., and the dependence of the susceptibility on temperature close to the Curie law.

The only compound of essentially tetrahedral distribution of the ligands about the cupric ion available was Cs_2CuCl_4, which has been shown [19] to have a tetrahedron of chlorine atoms, around the cupric ion, slightly flattened so as to destroy the three-fold rotation axis but retain the four-fold rotation-reflection property (S_4 axis) of the tetrahedron. The moment of this compound is, indeed, a little higher than those of the other cupric compounds studied, at 2·0 B.M., but it is doubtful if much significance could be attached to the small difference. The magnetic behaviour conforms closely to Curie's law, with $\theta = 1°$. These results are not in good agreement with the properties expected for the cupric ion in a tetrahedral environment as outlined above, but could be understood if the departure from tetrahedral symmetry raised fairly large splittings of the ground-state d_ϵ levels, as is likely.

From these results and discussion it seems unlikely that the assignment of a tetrahedral stereochemistry to a number of cupric compounds made by Ray and Sen is justified. The magnetic properties of the cupric complexes studied have been found to be in accord with the presence of an octahedral or distorted octahedral arrangement (including square planar). The Curie law has been found to hold, even when the stereochemistry approximated to tetrahedral. It seems likely that many of the high values of θ reported by Ray and Sen are not real.

The curvature noticeable at high temperatures for most of the plots of Figs. 2—4 are due to the presence of a temperature-independent paramagnetism ($N\alpha$ term) of the same form as that reported [12] for $K_2Cu(SO_4)_2,6H_2O$ and calculated [5] for $CuSO_4,5H_2O$, and also noticed in spin-paired cobaltous complexes.[16] The value of $N\alpha$ found was mostly around 60×10^{-6} in the molar susceptibility, *i.e.*, just the values previously reported and calculated. The $N\alpha$ term arises from second-order interactions through the magnetic field between the d_γ and d_ϵ levels, and is expected to remain substantially the same while either of the d_γ orbitals lies lowest—as in any form of octahedral or square planar stereochemistry. The magnitude of the effect when the d_ϵ orbitals lie lowest cannot be estimated without a detailed knowledge of the ground state and consequently it is not possible to comment on the absence of the effect in tetrahedral Cs_2CuCl_4. This is especially so because the effect is also inexplicably absent from $CsCuCl_3$, and from Cu(acetylacetone)$_2$.

Experimental

The measurements of the magnetic susceptibilities at various temperatures were made on the equipment described in Part I.[16]

The preparation and properties of the compounds $Cu(o\text{-phenanthroline})_3(ClO_4)_2$, $Cu(o\text{-phenanthroline})_2Br(ClO_4)$, $Cu(o\text{-phenanthroline})_2Br_2$, $Cu(o\text{-phenanthroline})_2(ClO_4)_2$, and $Cu(dipyridyl)_3(ClO_4)_2$ will be published elsewhere by one of the authors (C. M. H.).

Cu(dimethylglyoxime)Cl_2 was prepared by mixing concentrated solutions of cupric chloride and dimethylglyoxime in equimolecular proportion in alcohol at the b. p. (Found: Cu, 25·3; Cl, 28·3. Calc. for $CuC_4H_8O_2N_2Cl_2$: Cu, 25·36; Cl, 28·50%).

$CsCuCl_3$ was prepared by evaporating to crystallisation an aqueous solution containing equimolecular proportions of CsCl and $CuCl_2$ (Found: Cu, 20·9. Calc. for $CsCuCl_3$: Cu = 20·98%).

[17] Martin, unpublished work.
[18] Koyama, Saito, and Kuroya, *J. Inst. Polytechnic Osaka City Univ.*, 1953, **4**, 43.
[19] Helmholtz and Kruh, *J. Amer. Chem. Soc.*, 1952, **74**, 1176.

Cs_2CuCl_4 was prepared in the same way by employing a molar ratio of CsCl : $CuCl_2$ of 2 : 1 (Found: Cu, 13·4. Calc. for Cs_2CuCl_4: Cu, 13·47%).

The authors are indebted to Mrs. S. Djordjevic for the loan of the sample of Cu(acetylacetone)$_2$ (Found: Cu, 24·3; C, 45·73; H, 5·45. Calc. for $CuC_{10}H_{14}O_4$: Cu, 24·3; C, 45·9; H, 5·39%).

The authors are indebted to Professor R. S. Nyholm and Dr. J. Lewis for valuable discussions and suggestions during the preparation of this manuscript, and to Dr. R. L. Martin for permission to quote the result of the measurement on Cu(glycine)$_2$,H_2O.

William Ramsay and Ralph Forster Laboratories,
University College, London,
University of Sydney, New South Wales. [*Received, August 6th,* 1958.]

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176. *Oxomanoyl Oxide.*

By P. K. Grant.

The position of the carbonyl group in oxomanoyl oxide has been confirmed. The six-membered oxide ring shows two characteristic infrared absorption bands, at 1117—1120 and 1076—1080 cm.$^{-1}$.

Hosking and Brandt [1] assigned structure (I) to oxomanoyl oxide. This compound yielded a hydroxymethylene derivative (presumably the mono-derivative) on treatment with ethyl formate, despite the presence of two methylene groups adjacent to the ketonic group, but their isolation of 1 : 2 : 5 : 7-tetramethylnaphthalene on selenium dehydrogenation of its methyl Grignard derivative proved the 3-position of the keto-group.

Since this investigation, no other diterpene has been shown conclusively to be oxygenated in ring A, but all similarly oxygenated triterpenes have the oxygen atom, usually as hydroxyl, adjacent to the *gem.*-dimethyl group. By analogy the possibility that oxomanoyl oxide was oxygenated in the 2-position warranted investigation. The 2-position also offered the possibility of a different biosynthetic process,[2] namely cyclisation by OH^+ (as for triterpenes) of the necessary isoprenoid units rather than the normal H^+-cyclisation of diterpenes.

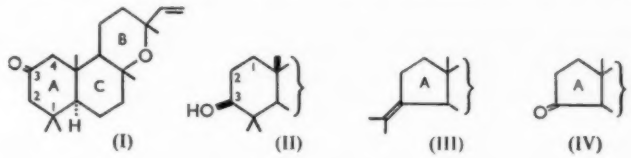
Chemical and physical studies were undertaken to distinguish between the two alternative structures of oxomanoyl oxide. Catalytic reduction of the oxide gave dihydrooxomanoyl oxide which with sodium borohydride gave the two stereoisomers of dihydrohydroxymanoyl oxide; these were also prepared *via* hydroxymanoyl oxide by treatment with these reducing agents in the reverse order.

Since the A/C ring-junction in the manoyl oxide series is *trans*,[3] a 3-hydroxyl group in the more stable equatorial conformation would have the α-configuration, whereas an equatorial 2-hydroxyl group would have the β-configuration. The stereoisomeric dihydrohydroxymanoyl oxides were separated chromatographically, the major component showing a C–O stretching band at 1039 cm.$^{-1}$, a frequency consistent with an equatorial hydroxyl group,[4] but the axial epimer showed an unusually high C–O stretching frequency (1030 cm.$^{-1}$).

The location of the hydroxyl group was shown by the standard reaction sequence [5] previously applied to triterpenes with 3β-hydroxy-groups (cf. II): dehydration with phosphorus oxychloride of such compounds is accompanied by ring contraction involving retropinacolinic rearrangement, and ozonolysis of the dehydration product (III) then yields acetone and the corresponding A-nor-ketone (IV). Now, dehydration of both

[1] Hosking and Brandt, *Ber.*, 1935, **68**, 286.
[2] Ruzicka, *Experientia*, 1953, **9**, 357.
[3] Jeger, Durst, and Buchi, *Helv. Chim. Acta*, 1947, **30**, 1853.
[4] Cole, Jones, and Dobriner, *J. Amer. Chem. Soc.*, 1952, **74**, 5571.
[5] Ruzicka, Montavon, and Jeger, *Helv. Chim. Acta*, 1948, **31**, 818; Dorée, McGhie, and Kurzer, *J.*, 1949, S167.

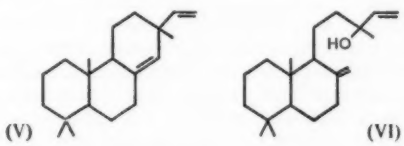
epimers of dihydrohydroxymanoyl oxide gave the same product, which showed a C:C stretching band at 1663 cm.$^{-1}$ but no band for a hydroxyl-group. A strong absorption band at 964 cm.$^{-1}$, together with lack of end absorption in the ultraviolet region,[6] strongly suggested the presence of a disubstituted ethylenic double bond: the dehydration product thus has a CH:CH group at position 2 : 3 or 3 : 4 in a six-membered ring A, consistent



(I) (II) (III) (IV)

with structure (I) for oxomanoyl oxide and inconsistent with a 2-oxo-group, for in the latter case the dehydration product (III) would contain a tetrasubstituted ethylenic linkage. Ozonolysis of the dehydration product gave no acetone or other volatile carbonyl product, and the ozonolysis product, although not crystalline, showed absorption bands at 1703 and 1723 cm.$^{-1}$, possibly corresponding to expectations for an aldehydic carboxylic acid. The absence of a carbonyl band in the 1740 cm.$^{-1}$ region eliminated the possibility that the ozonolysis product was a *cyclo*pentanone (IV), the end product from a 2-ketone in this reaction sequence.

From a study of the infrared spectra of these derivatives of manoyl oxide and of the closely related compounds rimuene (V) and tetrahydrorimuene it has been possible to attribute a characteristic frequency to the oxide ring in the manoyl oxide type compounds. The series manoyl oxide, dihydromanoyl oxide, oxomanoyl oxide, dihydro-oxomanoyl oxide, hydroxymanoyl oxide, dihydrohydroxymanoylol oxide, and the dehydration product of dihydrohydroxymanoyl oxide all showed two strong bands, at 1117—1120 and 1076—1080 cm.$^{-1}$ respectively, both of which were absent from the spectra of rimuene, tetrahydrorimuene, and manool (VI) where the oxide ring is not present. The former band, the characteristic C–O stretching band, is in the range 1150—1060 cm.$^{-1}$ attributed to alkyl ethers.[7] The doublet is also present in the ozonolysis product.



(V) (VI)

It was hoped that by measuring the peak intensity of the band resulting from methylene groups adjacent to the oxo-group [8] of oxomanoyl oxide a physical proof of the position of this group could be obtained. Measurements were carried out on dihydro-oxomanoyl oxide in order to eliminate the interference of the 1418 cm.$^{-1}$ CH_2 in-plane deformation band of the vinyl side chain, but the intensity of the " perturbed CH_2 vibration " at 1422 cm.$^{-1}$ showed little correlation with the intensities of similar bands in the reference compounds cholestanone, lanostenone, and β-amyrone.

Experimental

M. p.s are corrected. Unless otherwise stated, light petroleum had b. p. 40—60°.

Fractional distillation, under reduced pressure, of an acetone extract of the heartwood of *Dacrydium colensoi* yielded oxomanoyl oxide, b. p. 170—180°/0·4 mm. The ether–light petroleum eluate from a chromatogram of this oil on alumina (grade 1) gave oxomanoyl oxide,

[6] Halsall, *Chem. and Ind.*, 1951, 867.
[7] Bellamy, " The Infrared Spectra of Complex Molecules," Methuen, London, 1955, p. 101.
[8] Jones and Cole, *J. Amer. Chem. Soc.*, 1952, **74**, 5648.

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m. p. 77—78° (from aqueous methanol) (lit., b. p. 174—178°/0·5 mm.; m. p. 76—77°), $\nu_{max.}$ (in Nujol) 3044w, 1703s, 1635, 1419, 1348w, 1310w, 1295w, 1282s, 1264, 1224, 1212, 1190w, 1166, 1155, 1140, 1120s, 1097, 1080s, 1041s, 1023, 1016, 996, 985, 968, 923s, 892w, 863, 847 cm.$^{-1}$.

Dihydro-oxomanoyl Oxide.—Oxomanoyl oxide (200 mg.) in methanol (25 c.c.) was hydrogenated in the presence of Adams catalyst (uptake 15·4 c.c. at 20°/766 mm., equiv. to one double bond). Removal of the methanol in a vacuum and chromatography of a light petroleum solution of the product yielded dihydro-oxomanoyl oxide (150 mg.), m. p. 91—92° (from aqueous methanol) (lit., 89—90°), $\nu_{max.}$ (in Nujol) 2720w, 1703s, 1345w, 1314w, 1299w, 1284s, 1265w, 1224, 1208, 1196w, 1177w, 1120s, 1109w, 1080s, 1056w, 1035, 996s, 988w, 960, 957, 912w, 891w, 863w, 840, 777w, 754w, 722, 705w, 690w cm.$^{-1}$, (in CCl_4) 1485, 1466s, 1422, 1394s, 1376s, 1369sh cm.$^{-1}$.

Dihydrohydroxymanoyl Oxide.—Dihydroxy-oxomanoyl oxide (1·77 g.) in methanol (30 c.c.) was reduced with sodium borohydride, the excess of hydride being destroyed with a few drops of glacial acetic acid. After dilution and removal of the methanol in a vacuum the mixture was extracted with ether to give a clear glass (1·87 g.). A light petroleum solution of the product was chromatographed on alumina (grade 1). A light petroleum–ether (5 : 1) eluate gave a colourless oil which on recrystallization from aqueous methanol yielded needles of dihydrohydroxymanoyl oxide (axial epimer), m. p. 79·5—80·5°. A light petroleum–ether (2 : 1) eluate gave needles of *dihydrohydroxymanoyl oxide (equatorial epimer)*, m. p. 51—52° after recrystallisation from aqueous methanol (Found: C, 77·85; H, 11·7. $C_{20}H_{36}O_3$ requires C, 77·85; H, 11·8%), $\nu_{max.}$ (in Nujol) 3370s, 1348w, 1314w, 1295w, 1225, 1200w, 1192, 1150w, 1140w, 1119s, 1093w, 1080s, 1039s, 1005, 994, 956, 929w, 909w, 889w, 835, 812 cm.$^{-1}$.

Hydroxymanoyl Oxide.—Oxomanoyl oxide (0·7 g.) in methanol (25 c.c.) was reduced with sodium borohydride, and the mixture worked up as before. The product was purified by chromatography on alumina but separation into stereoisomers was not attempted at this stage.

Recrystallisation of the product (0·6 g.) from aqueous methanol gave colourless needles of *hydroxymanoyl oxide*, m. p. 80—81° (a mixed m. p. with oxomanoyl oxide gave a 20° depression) (Found: C, 78·3; H, 10·9. $C_{20}H_{34}O_2$ requires C, 78·4; H, 11·2%), $\nu_{max.}$ (in Nujol) 3400s, 3062w, 1644, 1490, 1413, 1365, 1321, 1311w, 1289, 1256, 1222, 1198, 1190, 1168w, 1136, 1117s, 1100s, 1076s, 1041w, 1025s, 1000sh, 944s, 928w, 918s, 904, 887, 837s, 810, 797w, 745w, 721w, 703, 668w, 652 cm.$^{-1}$. Hydrogenation of this oxide (122 mg.) in methanol (20 c.c.) in the presence of Adams catalyst (uptake 7·6 c.c., 20°/764 mm., equiv. to one double bond) gave, after removal of the methanol in a vacuum and chromatography of the product on alumina (grade 1), the epimeric dihydrohydroxymanoyl oxides, m. p. and mixed m. p. 79° and 51° respectively.

Dehydration of Dihydrohydroxymanoyl Oxide.—Phosphorus oxychloride (10 c.c.) was added dropwise to a solution of dihydrohydroxymanoyl oxide (0·52 g.) in pyridine (30 c.c.). The mixture was heated on a water-bath for ½ hr., kept overnight, and re-heated on a water-bath for ½ hr. Dilution with water and ether-extraction gave sticky crystals which were chromatographed on alumina (grade 1) in light petroleum. A light petroleum eluate gave colourless needles of the dehydration product (0·32 g.), m. p. 83—84° after recrystallisation from methanol (Found: C, 82·4; H, 11·7. $C_{20}H_{34}O$ requires C, 82·65; H, 11·8%), $\lambda_{max.}$ 205, 210, 215, 220, 223 mμ (ε 708, 152, 54, 38, 30), $\nu_{max.}$ (in Nujol) 1660, 1359, 1324w, 1305, 1277w, 1262, 1236w, 1222, 1199, 1166, 1120s, 1077s, 1068w, 1038s, 1005, 994s, 984s, 964, 954, 946, 928w, 910w, 903, 887, 847s, 807w, 774w, 760w, 733s, 724s cm.$^{-1}$.

The following spectra were also recorded:

Manoyl oxide, m. p. 29°, $\nu_{max.}$ (film) 2934s, 2872, 1649, 1469s, 1446, 1389s, 1366, 1336w, 1311w, 1295w, 1250, 1224w, 1206w, 1193w, 1175w, 1151, 1126w, 1119s, 1102, 1079s, 1045, 1030, 1018, 995, 988, 973, 963w, 918s, 859w, 841w, 814w, 700w, 683w, 669w cm.$^{-1}$.

Dihydromanoyl oxide, m. p. 19°, $\nu_{max.}$ (film) 2926s, 2864, 1463, 1387, 1374, 1352w, 1338w, 1311, 1294, 1275w, 1264, 1243w, 1212w, 1202, 1188, 1146, 1117s, 1090, 1080s, 1070w, 1054w, 1044, 1035, 1025w, 1005s, 985w, 970s, 959s, 931, 903w, 887w, 857, 844, 831w, 814w, 782w, 699, 673 cm.$^{-1}$.

Manool, m. p. 53°, $\nu_{max.}$ (in Nujol) 3390s, 1643, 1409w, 1345w, 1315w, 1271w, 1254w, 1222w, 1202, 1190, 1138w, 1115w, 1101, 1037, 988s, 913s, 888s, 735, 675 cm.$^{-1}$.

The author thanks Professor E. R. H. Jones for a sample of β-amyrone, Professor D. H. R. Barton for samples of cholestanone and lanostenone, and Mr. Seelye for samples of rimuene and

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tetrahydrorimuene. Microanalyses were carried out by Dr. A. D. Campbell, Otago University. Thanks are also offered to Mr. R. Fraser, Dominion Laboratory, for determination of infrared spectra and to Mr. I. R. McDonald, Dominion Laboratory, for helpful discussions.

DOMINION LABORATORY, DEPARTMENT OF SCIENTIFIC & INDUSTRIAL RESEARCH,
WELLINGTON, NEW ZEALAND. [*Received, September 12th*, 1958.]

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177. *The Solubility Behaviour of Aromatic Hydrocarbons in Benzene.*

By E. MCLAUGHLIN and H. A. ZAINAL.

The solubilities in benzene have been determined between room temperature and approximately 80° for diphenyl, *o*-, *m*-, and *p*-terphenyl, 1 : 3 : 5-triphenylbenzene, naphthalene, anthracene, phenanthrene, pyrene, triphenylene, chrysene, fluoranthene, fluorene, and acenaphthene. For the compounds melting below approximately 150° a single curve is obtained when log mole fraction is plotted against T_f/T, where T_f and T are the melting point and solution temperature respectively. This general solubility behaviour of these compounds is interpreted with reference to the entropy of fusion rather than the customary heat of fusion. To test the solutions for strictly regular behaviour the interchange energies of the various solutes with benzene are derived from activity coefficients when calorimetric heats of fusion are known.

THERE has hitherto been no systematic study of the solubility behaviour of aromatic hydrocarbons in one solvent. Limited data are however available [1] for a few hydrocarbons in different solvents. In view of the importance of these compounds a detailed study of their behaviour in the same solvent was undertaken to obtain information on the influence of structure on solubility. The compounds are representative of three series of aromatic structures, the directly linked phenyl series, the *ortho*-fused benzene series and the fused benzene series with one five-membered ring which are important coal-tar constituents.

EXPERIMENTAL

Materials.—Sources of materials and m. p.s of the purified products are: pyrene 150·2°, triphenylene 198·1° (Rutgerswerke A.G.), fluorene 113·2°, fluoranthene 110·2°, diphenyl 68·9°, acenaphthene 94·1°, chrysene 254·0° (Gesellschaft für Teerverwertung), phenanthrene 98·4° (Synthetic Fuels Research Branch, Bureau of Mines, U.S.A.), *o*-terphenyl 55·5° (Eastman Kodak), *m*-terphenyl 87·0°, *p*-terphenyl 213·0°, naphthalene 80·1° (B.D.H.). 1 : 3 : 5-Triphenylbenzene, m. p. 174·9°, was synthesised by the method of Vorländer, Fischer, and Willie.[2] All the compounds were purified by chromatography on alumina with benzene as eluant, except that hot toluene was used for chrysene and light petroleum for *o*- and *m*-terphenyl. Chromatography was followed by recrystallisation. Solvents were removed by sublimation at 10^{-4} mm. and when the compounds did not sublime by prolonged heating *in vacuo* near the m. p. " AnalaR " benzene which had been dried over sodium wire and freshly distilled was used as solvent.

Apparatus and Technique.—The solubilities were determined by noting the solution temperatures of fixed mole fractions. The mixtures were made up by weight in Pyrex tubes which were then attached to a silica gel drying train. After being embedded in solid carbon dioxide the tubes were sealed at atmospheric pressure. Sealing at atmospheric pressure with liquid nitrogen as coolant frequently led to violent explosions with some compounds, often up to half a day after return to room temperature; no combustion was evident after the explosions; purging the tubes with oxygen-free nitrogen before adding the hydrocarbons did not eliminate the effect.

[1] Seidell, " Solubilities of Organic Compounds," D. Van Nostrand & Co., New York, 1941.
[2] Vorländer, Fischer, and Willie, *Ber.*, 1929, **62**, 2836.

The solution temperatures were determined by rotating the tubes in a thermostat and noting the temperature at which the last trace of solid dissolved. The thermostat was controlled electrically to $\pm 0{\cdot}05°$ and temperatures were determined to the nearest $0{\cdot}1°$ with N.P.L. certified thermometers. In general a rough estimate of each solution temperature was first obtained and then approached in $0{\cdot}1°$ steps. Table 1 lists the solubilities found.

TABLE 1. *Solubilities of aromatic hydrocarbons in benzene.*

[x = *mole fraction*; *temp.* (T) *in* ° C.]

Diphenyl	T	37·0°	47·6°	59·2°	63·2°		
	x	0·5118	0·6478	0·8195	0·8916		
o-Terphenyl	T	28·0°	32·4°	44·8°	50·4°		
	x	0·5852	0·6442	0·8102	0·9013		
m-Terphenyl	T	36·8°	47·0°	60·8°	67·4°	74·2°	77·6°
	x	0·2827	0·3838	0·5466	0·6407	0·7571	0·8344
p-Terphenyl	T	38·0°	60·2°	64·2°	68·0°	77·6°	
	x	0·0071	0·0156	0·0178	0·0204	0·0279	
1 : 3 : 5-Triphenylbenzene	T	25·2°	28·6°	40·4°	46·2°	59·4°	66·6°
	x	0·0299	0·0351	0·0483	0·0562	0·0795	0·0960
Naphthalene	T	35·0°	45·0°	47·4°	63·2°	75·8°	
	x	0·3766	0·4806	0·5094	0·7119	0·9180	
Anthracene	T	35·8°	42·4°	50·6°	59·6°	70·2°	
	x	0·0103	0·0130	0·0173	0·0225	0·0315	
Phenanthrene	T	32·0°	40·2°	41·8°	50·2°	58·0°	
	x	0·2239	0·2836	0·2990	0·3750	0·4572	
Pyrene	T	32·4°	58·6°	66·8°	76·2°	84·6°	
	x	0·0734	0·1506	0·1896	0·2441	0·3014	
Triphenylene	T	39·4°	47·6°	63·8°	69·4°	82·8°	
	x	0·0140	0·0181	0·0289	0·0341	0·0497	
Chrysene	T	35·6°	45·8°	60·6°	72·2°		
	x	0·0021	0·0032	0·0052	0·0079		
Fluorene	T	33·6°	54·4°	58·4°	69·4°	72·8°	
	x	0·1604	0·2778	0·3095	0·4059	0·4405	
Acenaphthene	T	30·6°	41·4°	63·2°	69·4°		
	x	0·1815	0·2540	0·4731	0·5552		
Fluoranthene	T	44·8°	56·0°	64·4°	77·2°		
	x	0·2174	0·3011	0·3826	0·5331		

DISCUSSION

The solubility of a solute of melting point T_t (° K) in a solvent at temperature T (° K) may be written:[3]

$$\ln 1/a = \frac{\Delta H_t}{\boldsymbol{R}} \cdot \left(\frac{1}{T} - \frac{1}{T_t}\right) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where a is the activity of the solute and ΔH_t the molar heat of fusion, at temperature T, of the pure solute. In an ideal solution, a is equal to x so that a plot of ln x against $1/T$ passes through the melting point and has a slope of $\Delta H_t/\boldsymbol{R}$.

For the present series (compounds with melting points below approximately 150°, *viz.*, naphthalene, phenanthrene, pyrene, acenaphthene, fluoranthene, fluorene, diphenyl, and *o*- and *m*-terphenyl) plots of log x against $1/T$ were linear, within experimental error, over the measured temperature range and on extrapolation passed through the melting point. Equations for the solubilities of these compounds were determined by the method of least squares subject to the condition that the equation satisfies the point $(0, 1/T_t)$.

Table 2 gives the parameters of the solubility equation:

$$\log x = -m(1/T) + C \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

for these compounds in benzene. Plots for the other molecules did not pass through the melting point on linear extrapolation and so have not been represented by parameters.

In all cases where heats of fusion are known (see Table 3) it was found that the solubility curves did not have slopes corresponding to ideal values. Reasons for these departures from ideality may be explained on the basis of regular solution theory.

[3] Hildebrand and Scott, "Solubility of Non-Electrolytes," Reinhold Publ. Corp., New York, 1950.

To test the solutions of aromatic hydrocarbons in benzene for strictly regular behaviour the interchange energy W can be derived when heats of fusion are known. The interchange energy is defined [4] such that if, on starting with two pure lattices of molecules A and B, an interior A molecule is exchanged with an interior B molecule the total increase of energy is $2W$, all molecules being assumed at rest on their lattice points. If the solutions are strictly regular then the interchange energy determined by the equation:

$$f = \exp[(1 - x)^2 W/kT] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

should be constant within the accuracy of the experimental data. Here f is the activity coefficient of the solute, so that W must be zero for an ideal solution with $f = 1$. In addition, in a strictly regular solution the solvent and solute molecules are assumed [4] to be sufficiently alike in size and shape to be interchangeable on a quasi-lattice. For spherical molecules this requires [4] a ratio of molecular volumes between 1 and 2.

TABLE 2. *Parameters of solubility equation.*

Compound	m	C	Compound	m	C
Phenanthrene	1075·5	2·891	Diphenyl	971·8	2·840
Naphthalene	1016·6	2·920	Fluoranthene	1241·8	3·247
Pyrene	1242·6	2·937	Fluorene	1159·6	2·989
o-Terphenyl	840·0	2·554	Acenaphthene	1302·7	3·547
m-Terphenyl	1208·7	3·358			

TABLE 3. *Heats and entropies of fusion of aromatic hydrocarbons.*

Compound	T_f (° K)	ΔH_f (cal./mole)	ΔS_f (cal. deg.$^{-1}$ mole^{-1})
Naphthalene [a]	353·5	4490	12·7
Anthracene [b]	489·2	6890	14·1
Phenanthrene [b]	372·3	4450	12·0
Diphenyl [c]	342·1	4460	13·0
Acenaphthene [d]	367·3	4950	13·5
Fluorene [e]	388·1	4800	12·4

[a] Ward, *J. Phys. Chem.*, 1934, **38**, 761. [b] Parks and Huffman, *Ind. Eng. Chem.*, 1931, **23**, 1138. [c] Spaght, Thomas, and Parks, *J. Phys. Chem.*, 1932, **36**, 882. [d] Skau, *ibid.*, 1935, **39**, 761. [e] Mortimer, *J. Amer. Chem. Soc.*, 1923, **45**, 633.

TABLE 4. *Interchange energy (W/k) of benzene with aromatic hydrocarbons.*

Compound	Molar volume (ml.) at T_f	Temp. (° C) 10°	20°	30°	40°	50°	60°
Fluorene	163·7	81	78	76	75	76	78
Acenaphthene	148·7	140	135	131	131	132	147
Phenanthrene	169·2	35	34	34	35	37	41
Anthracene	178·9	134	130	128	128	127	129
Naphthalene	127·1	25	25	26	28	33	43

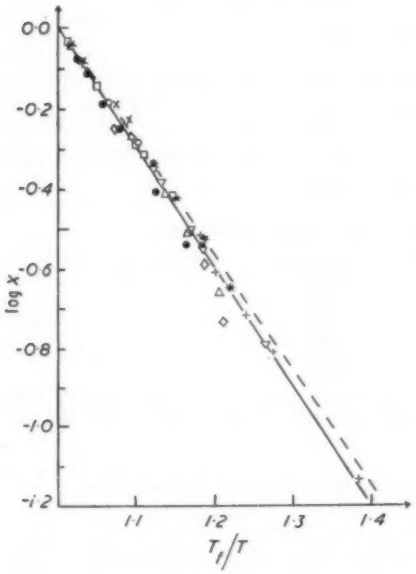
Table 3 gives values of the known heats of fusion of the compounds and Table 4 the values of W/k (° K) determined from these values and the experimental solubilities at 10° intervals. The solubilities were interpolated by using equation (2), and variation of the heat of fusion has been neglected as a first approximation. W/k has not been derived for diphenyl owing to some uncertainty about the value of the latent heat of fusion.[5]

Examination of the values for W/k given in Table 4 shows that the solutions conform roughly to regular behaviour, W/k being constant within an average of 4% over the measured range. Deviations from ideal behaviour may therefore be attributed to the existence of a finite interchange energy on mixing the solvent and solute quasi-lattices.

Although the molecules listed in Table 4 are mostly planar their volumes are approximately twice that of the solvent molecules (benzene has mol. vol. 87·3 ml.) at the melting

[4] Guggenheim, "Mixtures," Oxford Univ. Press, 1952.
[5] Warner, Scheib, and Svirbely, *J. Chem. Phys.*, 1934, **2**, 590.

point, so that conformity to strictly regular behaviour may seem a little surprising. However, from an examination of the volume requirements for rotation about the three principal axes it has been shown [6] that the fused-ring aromatic hydrocarbons do not, on an average, have sufficient room in the liquid state to assume completely random configurations. As the volume for rotation about the axis in the plane of the molecule is generally much greater than the molar volume of the liquid the molecules adopt a quasi-parallel configuration in the liquid state over small regions. This is borne out by the *X*-ray structure of liquid benzene [7] and by the relatively low viscosities of melts of aromatic hydrocarbons.[6] In these layer liquids the interlayer distance should be approximately constant whatever the molecule, so that mixtures with benzene are " two-dimensional " solutions. This peculiarity may facilitate conformity to regular solution behaviour despite the difference in molecular volume between solvent and solute.



Plot of log *x against* T_f/T.

□ *Naphthalene.* ○ *Diphenyl.* ▽, Fluorene. ◇, Acenaphthene. ×, *o*-Terphenyl. +, Pyrene. △, Fluoranthene. ●, *m*-Terphenyl. ✱, Phenanthrene. *Ideal solubility curve* — — —.

To examine the general pattern of the solubility of these aromatic hydrocarbons in benzene and the effect of structure on solubility equation (1) may be transformed into

$$\ln a = -\Delta S_f[(T_f/T)-1]/R \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

by multiplying the right-hand side above and below by T_f and rearranging the result. Here ΔS_f is the molar entropy of fusion. It is seen from Table 3 that the average molar entropy of fusion is $13{\cdot}0 \pm 0{\cdot}6$, in agreement with Walden's rule [8] which predicts this value for many compact organic molecules. As the solubility curves pass through the point $(0, 1/T_f)$ of plots of log x against $1/T$(° K) and are linear for compounds melting below approximately 150°, a plot of ln a for each substance against T_f/T would be expected to fall on a single curve with a slight scatter due to small deviations from the average entropy of fusion.

[6] McLaughlin and Ubbelohde, *Trans. Faraday Soc.*, 1957, **53**, 628.
[7] Pierce, *J. Chem. Phys.*, 1937, **5**, 717.
[8] Walden, *Z. Elektrochem.*, 1908, **14**, 713.

No independent data on the saturation activity coefficients obtained by other techniques are available, so that equation (4) cannot be directly tested. However, if log x is plotted against T_t/T it is found that the data for these compounds melting below 150° lies on a single curve. This is illustrated in the Figure where the best straight line, subject to the condition that it passes through the point (1, 0), has been fitted by the method of least squares. The ideal curve ΔS_t, being taken as 13·0 molar entropy units, is also shown. For compounds with melting points above 150° the scatter (not shown) from the best straight line is somewhat greater. This is probably due to the relatively larger heats and entropies of fusion of these compounds (cf. anthracene in Table 3). As a first approximation, nevertheless, the solubility of all the aromatic hydrocarbons in benzene studied can be represented approximately by the equation:

$$\log x = -\frac{13{\cdot}8}{2{\cdot}303R} \cdot \left[\frac{T_t}{T} - 1\right] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

Solubilities calculated from equation (5) agree with experimental values, on an average, within about 5% for compounds melting below 150° but for higher-melting compounds may be in error by a factor of three.

The limited solubility data available for the low-melting compounds in carbon tetrachloride also fall on a single line in a plot of log x against T_t/T. This indicates a similarity in the entropy of solution of these compounds in non-polar solvents. In alcohol the plots are different for each compound and non-linear in general, indicating other factors as operative.

In the absence of solubility data for aromatic hydrocarbons in any solvent where deviations from ideality are expected to be small, the entropy term in equation (5) can be assumed to have an ideal value of 13, to afford an estimate of the solubility from the melting point alone.

Two well-known generalisations concerning the solubility of solids can be made [3] from the ideal solubility equation which is obtained from equation (1) when $a = x$: (1) If the heats of fusion of two substances are similar the one with larger T_t should have the smaller solubility in any solvent. (2) If two solids have similar melting points the one with lower ΔH_t should be the more soluble. However, as the melting point is a function of the lattice cohesion energy of the solid, such rules give no information on the effect of structure on solubility except in so far as structure influences the melting point. For example, any branched terphenyl has a much lower melting point that the straight-chain member and would therefore have a greater solubility; also the more compact a fused-ring system the lower its melting point and hence the greater its solubility, as, for example, with pyrene and triphenylene. However, the Figure brings out the point that if solubilities of all these compounds, both fused and directly linked, are compared at the same reduced temperature T/T_t they all have the same solubility, irrespective of their structure.

Thanks are offered to Professor A. R. Ubbelohde, F.R.S., for helpful advice and encouragement and to the National Coal Board for financial support for chemicals. One of us (H. A. Z.) thanks the Government of Iraq for a grant.

Department of Chemical Engineering, Imperial College,
South Kensington, London, S.W.7. [*Received, October 3rd,* 1958.]

XUM

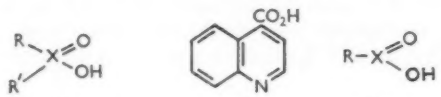
178. *Infrared Spectra and Hydrogen Bonding in Compounds containing* X(:O)·OH *Groups.*

By JOHN T. BRAUNHOLTZ, G. E. HALL, FREDERICK G. MANN, and N. SHEPPARD.

A well-defined absorption pattern, consisting of a characteristic trio of very broad bands in the regions 2800—2400 (*A*), 2350—1900 (*B*), and 1720—1600 cm.$^{-1}$ (*C*), appears to provide a reliable criterion for the presence of the structural grouping X(:O)·OH, and to be largely independent of the nature of the central atom X. Examples are cited for X = P, As, S, and Se and, less commonly, C. These bands are undoubtedly associated with vibrations of the OH groups under conditions of strong hydrogen bonding; it is suggested that *A* and *B* correspond to ν OH and *C* to δ OH vibrations. Band *C* is variable in intensity, and is sometimes weak when two OH groups are attached to X, as in organic phosphonic and arsonic acids.

In certain cases these characteristic bands are not observed despite the presence of X(:O)·OH groups, *e.g.*, in the spectra of most carboxylic acids, presumably owing to the occurrence of different patterns of hydrogen bonding.

THE infrared spectra between 4000 and 1500 cm.$^{-1}$ of dibenzyl hydrogen phosphate (I; X = P, R = R′ = O·CH_2Ph), diphenylphosphinic acid (I; X = P, R = R′ = Ph), methylphenylarsinic acid (I; X = As, R = Me, R′ = Ph), cinchoninic acid (II), and phenylarsonic acid (I; X = As, R = Ph, R′ = OH) are shown in Fig. 1. The relative



(I) (II) (III)

widths of the bands are emphasised by adopting the unusual convention of plotting the spectra on a uniform scale of cm.$^{-1}$ throughout.

We draw attention to the characteristic trio of very broad absorption bands near 2600, 2200, and 1700 cm.$^{-1}$ (subsequently referred to as *A*, *B*, *C*, respectively), each extending over approximately 250 cm.$^{-1}$, which occur strongly in all the spectra except that of the arsonic acid, where band *C* is weaker than *A* and *B*. The same pattern of bands has been observed in the spectra of other phosphinic (I; X = P, R and R′ = alkyl or aryl) and arsinic acids (I; X = As, R and R′ = alkyl or aryl) studied during the present work. *iso*Nicotinic, quinaldinic, and cinchoninic acids are unusual examples of carboxylic acids which also show the *A*, *B*, *C* pattern of absorption bands. Amino-acids containing more basic nitrogen atoms occur usually in the zwitterionic form, but in the above examples a relatively sharp carbonyl absorption band occurs near 1700 cm.$^{-1}$ superimposed on the broad band *C*, indicating that the carboxyl group persists as such, although it is strongly hydrogen bonded, probably with the nitrogen atom of another molecule. Analogous spectroscopic phenomena have been briefly reported for polycyclic derivatives of cinchoninic acid.[1,2] In this region carboxylic acids which do not contain nitrogen atoms usually give a quite different spectrum, associated with dimeric hydrogen bonded units.[3]

The pattern *A*, *B*, *C* of absorption bands has been observed previously in the spectra of other phosphinic acids[4] (I; X = P, R = H, R′ = alkyl or aryl), disubstituted phosphates[4-7]

[1] Braunholtz and Mann, *J.*, 1958, 3368.
[2] *Idem*, *J.*, 1958, 3377.
[3] Bratož, Hadži, and Sheppard, *Spectrochim. Acta*, 1956, **8**, 249.
[4] Daasch and Smith, *Analyt. Chem.*, 1951, **23**, 853.
[5] Bellamy and Beecher, *J.*, 1952, 1701.
[6] Bellamy and Beecher, *J.*, 1953, 728.
[7] Maarsen, Smit, and Matze, *Rec. Trav. chim.*, 1957, **76**, 713.

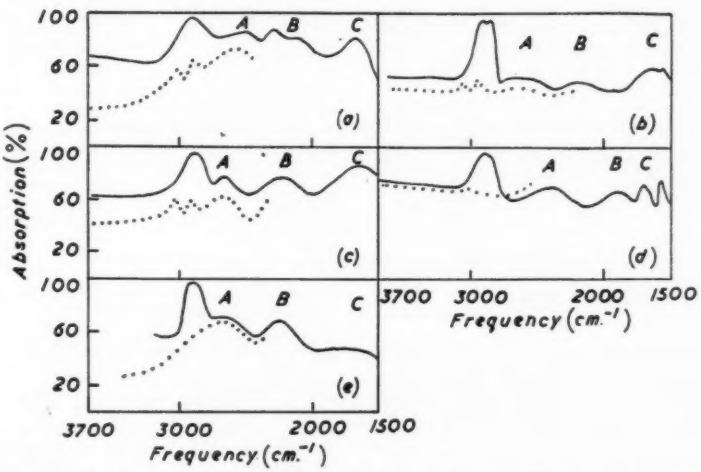
(I; X = P, R and R′ = OAlkyl or OAryl), and seleninic acids [8] (III; X = Se, R = aryl); the bands are also present in the spectra of sulphinic acids [9,10] (III; X = S, R = aryl) although band *C* is very weak in this case. Other examples are to be found in published spectra of a variety of inorganic acid salts, such as those containing HPO_4^{2-}, $H_2PO_4^-$, and $H_2AsO_4^-$ anions.[11-13]

Experimental data obtained in the present and previous work are given in the Table. An examination of these leads to the following generalisations:

(1) The presence of the complete trio of bands (*A*, *B*, *C*) appears always to indicate the presence of the structural group X(:O)·OH. The Table gives examples for X = P, As, S, Se, and C.

(2) The presence of the group X(:O)·OH does not, however, necessarily produce in the spectrum any or all of the bands *A*, *B*, and *C*. Thus, the bands are not shown by dimeric carboxylic acids,[3] liquid nitric or sulphuric and solid perchloric acids,[14] seleninic acid,[8] and phenylstibonic acid; the spectra of all these compounds have less broad OH absorption bands at somewhat higher frequencies.

FIG. 1. *The infrared spectra, in the region* 3700—1500 *cm.*$^{-1}$, *of* (*a*) *dibenzyl hydrogen phosphate* (I; X = P, R = R′ = O·CH_2Ph), (*b*) *diphenylphosphinic acid* (I; X = P, R = R′ = Ph), (*c*) *methylphenylarsinic acid* (I; X = As, R = Me, R′ = Ph), (*d*) *cinchoninic acid* (II), *and* (*e*) *phenylarsonic acid* (I; X = As, R = Ph, R′ = OH).



The use of a Nujol mull is denoted by (——), *and of a hexachlorobutadiene mull by* (. . . . . .).

(3) Among the organic derivatives band *C* is usually missing or ill-defined in comparison with *A* and *B* when a second hydroxyl group is attached to *X*. This behaviour is shown, for example, by the phosphonic and arsonic acid (I; X = P or As, R = OH, R′ = alkyl or aryl; Fig. 1) and the dihydrogen phosphates [5] (I; X = P, R = OH; R′ = OAlkyl or OAryl). Inorganic ions behave less regularly in this respect, for $H_2PO_4^-$ and $H_2AsO_4^-$ (Fig. 2) show band *C* strongly, whereas it appears to be weak in the spectrum [11] of HSO_4^-. It is probable that the detailed hydrogen-bonding pattern, as influenced by the second hydroxyl group, is responsible for these differences.

[8] Detoni and Hadži, *J. Chim. phys.*, 1956, **53**, 760.
[9] Guryanova and Syrkin, *Zhur. fiz. Khim.*, 1949, **23**, 105.
[10] Detoni and Hadži, *J.*, 1955, 3163.
[11] Miller and Wilkins, *Analyt. Chem.*, 1952, **24**, 1253.
[12] Corbridge and Lowe, *J.*, 1954, 493.
[13] *Idem*, *J.*, 1954, 4555.
[14] Bethell and Sheppard, unpublished work.

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(4) The trio of bands seems to be relatively independent of the other substituents on X, except when there is another hydroxyl group, as noted in (3).

Characteristic OH *absorption bands in the infrared spectra of compounds containing the group* X(:O)·OH.

Compound	Position of OH bands (cm.$^{-1}$) A	B	C
(*a*) X *carries one hydroxyl group.*			
(I; X = P)			
R = H, R′ = Ph [4]	2680	2300 *	1670 *
R = H, R′ = *p*-C_6H_4Me [4]	2640	2300 *	1670 *
R = H, R′ = *p*-C_6H_4Et [4]	2640	2300 *	1680 *
R = H, R′ = $C_{10}H_7$ † [4]	2550	2300 *	1650 *
R = R′ = Ph	2600	2200	1660
R = Ph, R′ = *m*-C_6H_4·OMe	2590	2260, 2150	1720
R = Ph, R′ = *o*-C_6H_4·OMe	2650	2150	1600
R = OMe, R′ = OEt [4]	2650	2300 *	1720 *
R = R′ = OPr^i [7]	2665	‡	1712
R = R′ = OBu^n [6]	2600	2280	1665
R = R′ = OBu^i [6]	2580	2160	1665
R = R′ = O·C_6H_{11} [6]	2590	2290	1665
R = R′ = O·C_6H_{11} [6]	2600	2220	1665
R = R′ = O·CH_2Ph (see also ref. 6)	2520	2280, 2150	1675
R = R′ = OPh (see also ref. 5)	2600	2100	1675
R = R′ = O·C_6H_4·NO_2-*p* [5]	2632	2353, 1923	1667
R = R′ = O·C_6H_4·OMe-*o* [5]	2632	2000	1639
R = R′ = O·$C_6H_2Cl_3$-2 : 4 : 6 [5]	2703	2353, 2174, 1942	1709
(I; X = As)			
R = Me, R′ = Ph	2700	2240	1675
R = Ph, R′ = CH_2Ph	2680	2340	1700
R = Ph, R′ = *m*-C_6H_4·NO_2	2670	2370, 2260	1705
(III; X = S) [10]			
R = Ph	2790 *	2340 *	1650 *
R = *p*-C_6H_4Me	2790 *	2340 *	1650 *
R = 2-$C_{10}H_7$	2790 *	2340 *	1700 *
(III; X = Se) [8]			
R = Ph	2720 *	2270 *	1660 *
R = *p*-C_6H_4Me	2720 *	2270 *	1660 *
(III; X = C)			
*iso*Nicotinic acid	2400	1972	1700
Quinaldinic acid	2500	1932	1690
Cinchoninic acid (II)	2370	1900	1715
(*b*) X *carries two hydroxyl groups.*			
(I; X = P, R = OH).			
R′ = *cyclo*Hexyl [5]	2667	2273	—
R′ = Bu^n [4]	2550, 2800	2300	—
R′ = Ph [4]	2690	2300	—
R′ = *p*-C_6H_4Cl [4]	‡	2300	—
R′ = O·$C_{18}H_{37}$ [6]	2700, 2500	2240	—
R′ = OPh § [5]	2667	2222	—
R′ = O·C_6H_4·C_8H_{17}-*p* [6]	2660	2220	—
(I; X = As, R = OH),			
R′ = Ph	2680	2280	1650 ‡
R′ = *p*-C_6H_4Me	2720	2290	1750 ‡
R′ = *o*-C_6H_4Me	2800	2340	—
R′ = *p*-C_6H_4Cl	2800	2340	1650 ‡
R′ = *o*-C_6H_4Br	2750	2320, 2180	1620 ‡
(*c*) *Inorganic compounds* [11]			
K_2HPO_4 *	2860	2380	1850
$BaHPO_4$ *	2700	2440, 2330	1720
$KHSO_4$ *	2860	2330	1640 ‡
KH_2PO_4 *	~2800	2330	1640
$(NH_4)H_2PO_4$ *	2860	2330	1640
KH_2AsO_4 (see also ref. 11)	2700	2300	1700
(*d*) *Compounds containing* X(:O)·OH *groups with exceptional* OH *frequencies.*			
Carboxylic acids (dimeric) [3]	*ca.* 3000		
(I; X = Sb, R = OH, R′ = Ph)	3200		
HNO_3 (liquid) [14]	*ca.* 3300, 3000, 2700		
H_2SO_4 (liquid) [14]	*ca.* 2900		
$HClO_4$ (solid) [14]	*ca.* 3300		
$NaHCO_3$ [11]	*ca.* (2900), 2500		
$KHCO_3$ [11]	*ca.* 2900, 2650		
(III; X = Fe) [9] (Lepidocrocite)	3395, 3125		
(III; X = Fe) [9] (Goethite)	3095		
(III; X = Mn) [9] (Manganite)	2625, 2040		
(III; X = Al) [9] (Diaspore)	2925, 2340, 2115, 1985		

* The position of the centre of these bands has been estimated from published data.
† The original authors do not specify α- or β-naphthyl.
‡ Band doubtful or very weak.
§ Hydrated.
[9] Cabannes-Ott, *Compt. rend.*, 1957, **244**, 2491.

The extremely broad bands under consideration are undoubtedly associated with vibrations involving hydroxyl groups which are concerned in very strong hydrogen bonding. Thus they disappear when the hydroxyl group is removed by salt formation,[8,10-13] and we have observed no such bands in the infrared spectrum of diphenylphosphinodithioic acid.

The higher-frequency bands *A* and *B* have been assigned with consistency to OH bond-stretching vibrations (νOH) by previous workers; however, conflicting assignments have been proposed for band *C*. Detoni and Hadži [8] in their study of seleninic acids suggest that *C* is another νOH band of surprisingly low frequency; Maarsen *et al.*[7] and Thomas [15] ascribe it on the other hand to an in-plane OH angle deformation vibration (δOH) of unusually high frequency. In either case strong hydrogen bonding could account qualitatively for the abnormal frequency.

We have now studied the spectrum of potassium dihydrogen arsenate and its dideutero-analogue. This pair of compounds was chosen because [11] no fundamental frequencies involving As–O or As=O bonds complicate the spectrum above 1000 cm.$^{-1}$. The spectrum of Fig. 2*a* is remarkable for the fact that, apart from a number of relatively shallow dips which define the " separate " bands in the absorption curve, there is almost continuous absorption from about 3000 cm.$^{-1}$ to 1000 cm.$^{-1}$. In addition to the bands *A*, *B*, and *C* this spectrum shows another broad band, *D*, near 1300 cm.$^{-1}$ which also has its origin in an OH vibration, for it shifts to considerably lower frequencies with deuteration. This band *D* is also discernible in the spectra of a number of organic molecules of the general type discussed here although it is then overlaid by much sharper absorption bands of the alkyl or aryl substituents.

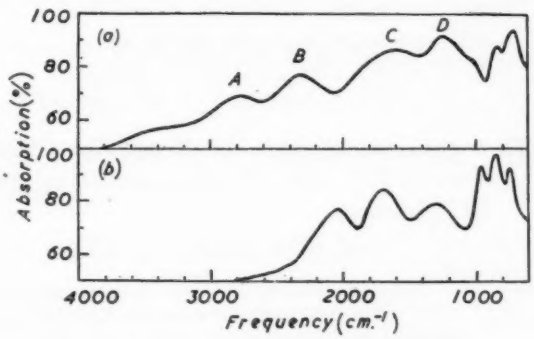

FIG. 2. *The infrared spectra of (a) potassium dihydrogen arsenate and (b) potassium dideuterium arsenate: both spectra are compounded from measurements with Nujol and hexachlorobutadiene mulls.*

Detoni and Hadži [8] have previously assigned band *D* in the spectrum of seleninic acids to a δOH vibration, and as it merges smoothly with band *C* we prefer the assignment of the latter to a δOH vibration also,[7,15] and the two higher-frequency bands *A* and *B* to νOH vibrations. It has been suggested [5,6] that compounds containing the P(:O)·OH group have δOH bands in the vicinity of 1030 cm.$^{-1}$; however, the evidence for this assignment is not clear-cut and has recently been challenged.[15] In most other types of compound hydrogen-bonded δOH vibrations have been assigned [16,17] to the general region 1500—1200 cm.$^{-1}$; a move to higher frequencies is not unexpected for conditions of exceptionally strong hydrogen bonding.

The fact that there are two νOH and two δOH absorption bands calls for comment. In the dihydrogen arsenate they agree with the presence of two OH groups in the ion; however, this cannot be the cause of the doubling, since the seleninic acids, with one hydroxyl group per molecule, show all four bands at similar positions.[8] Blinc and Hadži [18] made the interesting suggestion that the doubling of the νOH bands is caused by the unusual properties of a double-minimum potential-energy curve which may control the vibration of the hydrogen atoms; [19] however, this suggestion does not seem to explain readily the

[15] Thomas, *Chem. and Ind.*, 1957, 198.
[16] Stuart and Sutherland, *J. Chem. Phys.*, 1956, **24**, 559.
[17] Hadži and Sheppard, *Proc. Roy. Soc.*, 1953, *A*, **216**, 247.
[18] Blinc and Hadži, Proceedings of symposium on hydrogen bonding, Ljubljana, 1957, Pergamon Press (in course of publication); and personal communication.
[19] Kovner and Kapshtal, *Izvest. Akad. Nauk S.S.S.R., Ser. fiz.*, 1953, **17**, 561.

doubling of the δOH bands. Another possibility is that the doubling of both types of vibration frequency is caused by the exceptional coupling between adjacent ions through the strong hydrogen bonds. This explanation would be consistent with the *X*-ray crystal structures of dibenzyl hydrogen phosphate [20] and benzeneseleninic acid,[21] in which the hydrogen bonds couple the molecules together into spiral-type chains with two-molecule repeating units; on the other hand, a splitting of about 400 cm.$^{-1}$ in each case seems large for intermolecular effects. Finally, it is possible that some of these bands may represent overtones or combination frequencies of the lower-frequency δOH or γOH vibrations [3] (thus the *ca.* 2700 cm.$^{-1}$ band might correspond to the overtone of band *D*). Further experimental work is needed to distinguish between these possibilities.

Experimental

Potassium Dideuterium Arsenate.—Dry technical potassium dihydrogen arsenate (*ca.* 250 mg.) was dissolved in deuterium oxide (99·78%; 2 c.c.). The solvent was removed under vacuum, and the procedure was repeated with the solid residue. The dideuterium arsenate so obtained was stringently protected from atmospheric moisture before and during the preparation of the Nujol mull. Complete deuteration was confirmed by the absence of hydroxyl absorption bands from the infrared spectrum.

University Chemical Laboratory, Cambridge. [*Received, August 15th*, 1958.]

[20] Dunitz and Rollett, *Acta Cryst.*, 1956, **9**, 327.
[21] Bryden and McCullough, *ibid.*, 1954, **7**, 833.

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179. *Infrared Spectra of Transition Metal–Nitric Oxide Complexes. Part IV.* The Pentacyanonitrosyl-complexes of Chromium and Molybdenum.*

By W. P. Griffith, J. Lewis, and G. Wilkinson.

Infrared, polarographic, and magnetic-susceptibility measurements have been made on the new compound $K_3[Cr^{I}(CN)_5NO],H_2O$. On the basis of infrared spectral and other evidence we reformulate the previously reported $K_4[Mo^{0}(CN)_5NO],2H_2O$ as an octaco-ordinated bivalent molybdenum complex, $K_4[Mo^{II}(OH)_2(CN)_5(NO)]$; a known hydroxycyanomolybdate is also reformulated as $K_3[Mo^{V}(OH)_4(CN)_4],2H_2O$.

The use of hydroxylamine for the introduction of a nitrosyl group into transition-metal cyanide complexes has been known for some time.[1,2] A cyanomononitrosylchromium complex has been prepared by using conditions similar to those for the preparation of a molybdenum complex,[2] which was formulated as $K_4[Mo(CN)_5NO],2H_2O$. Whilst the chromium complex has an anion of stoicheiometry reported for this molybdenum compound, *i.e.* it is $K_3[Cr^{I}(CN)_5NO],H_2O$, infrared and other measurements lead us to reformulate the molybdenum complex with the metal atom having octaco-ordination, *i.e.* as $K_4[Mo^{II}(OH)_2(CN)_5(NO)]$.

Potassium pentacyanonitrosylchromate(I) *monohydrate*, $K_3[Cr(CN)_5NO],H_2O$. This compound was obtained by treating chromium trioxide in basic solution containing excess of cyanide ion with hydroxylamine. The bright green complex is very stable as a solid and in aqueous solution.

Magnetic-susceptibility measurements were made on the solid over a temperature range (Table 1); a plot of $1/\chi_A$ against T is linear and the calculated moment is 1·87 B.M.,

* Part III, *J.*, 1958, 3993.

[1] Hieber and Nast, *Z. anorg. Chem.*, 1940, **244**, 23; Hieber and Nast, *FIAT Review of German Science*, 1939—46, *Inorg. Chem.*, Part II, p. 146.
[2] Nast and Gehring, *Z. anorg. Chem.*, 1948, **256**, 169.

with a value of θ of $-7°$. The complex clearly has a single unpaired electron, in agreement with its formulation as a chromium(I) complex.

TABLE 1. *Magnetic susceptibility of solid* $K_3[Cr(CN)_5NO],H_2O$.

$T°$ (K)	295·6	265·0	230·0	198·0	158·0	124·0	85·0
$\chi_A \times 10^3$ (c.g.s.u.)	1·44	1·57	1·84	2·11	2·61	3·23	4·93
$1/\chi_A \times 10^3$ (c.g.s.u.)	6·95	6·35	5·45	4·75	3·83	3·10	2·03

Diamagnetic corrections were taken as -160×10^{-6} c.g.s.u.

There is an intense peak in the infrared spectrum (Table 2) at 1625 cm.$^{-1}$, which is quite different in appearance from that of H–O–H bending vibrations that also occur in this region, and is clearly assignable to an N–O stretching frequency. In the C–N stretching region there is a strong peak at 2137 cm.$^{-1}$ with a shoulder at 2095 cm.$^{-1}$, a structure found previously [3] in other complexes, *e.g.* $K_3[Co(CN)_5NO]$.

Polarographic reduction of a 0·01M-solution of the complex in aqueous 1M-potassium cyanide showed a well-defined wave corresponding to a one-electron reversible reduction. The half-wave potential was $-0·93$ v versus the standard mercurous chloride electrode. The product of the reduction must be $K_4[Cr^0(CN)_5NO]$, but attempts to isolate it have failed.

It is noteworthy that for the complexes $[M(CN)_5NO]$, the stability order is Fe(III) < Mn(II) < Cr(I); thus the iron complex exists only in solution and the manganese complex is very unstable. If we assume, with Pauling, that the bonds in this complex have about

TABLE 2. *Infrared spectra (cm.$^{-1}$) of chromium and molybdenum complexes.*

$K_3[Cr(CN)_5NO],H_2O$	2137vs, 2095sh, 1645vs CN str CN str NO str
$K_4[Mo(OH)_2(CN)_4NO]$ ...	3300—3500, 2130s, 2106s, 2081vs, 2062vs, 2037vs, 1595vs, 980m, 835b, OH str CN str NO str MoO str? 580m, 475m, 375w
$K_4[Mo(OH)_4(CN)_4]$	3300—3500, 2105s, 2083vs, 2055w, sh, 925w, 825b OH str CN str MoO str?
$K_2[Mo(OH)_4(CN)_4],2H_2O$	3300—3500, 2100s, 2080vs, 2055s, 925m, 825b OH str CN str MoO str?
$K_4[Mo(OH)_2(CN)_5],nH_2O$	3300—3500, 2106vs, 2058vs, 920m, 840sb OH str CN str MoO str?
$K_4[Mo(CN)_8],2H_2O$ * [a] ...	2118vs, 2096vs, 2050vs
$K_3[Mo(CN)_8],2H_2O$ * [a] ...	2118vs, 2096vs, 2045vs
$Na_2MoO_4,2H_2O$ † [b]	900m, 855m, 820s, b MoO str
$K_2MoO_4,5H_2O$ [14]	900m, 825s, b MoO str

* CN stretching region only is quoted.
† Absorption in 800—1000 cm.$^{-1}$ region only quoted; $PbMoO_4$ also absorbs in this region.
[a] Brane, Johnson, Larsen, and Meloche, *J. Inorg. Nuclear Chem.*, 1958, **6**, 99.
[b] Miller and Wilkins, *Analyt. Chem.*, 1951, **24**, 1253.

50% covalent character, the formation of six such bonds would lead to resultant charges of -2, -1, and 0 for the chromium, manganese, and iron complexes, respectively. The negative charge is dissipated, in agreement with Pauling's electroneutrality principle, by

[3] Griffith, Lewis, and Wilkinson, *J. Inorg. Nuclear Chem.*, 1958, **7**, 38.

the formation of π-bonds between the metal and the ligands. Thus the maximum π-bonding and stability would occur for chromium; the N–O stretching frequency accordingly decreases in the same order as the increased metal–ligand double bonding.

Potassium dihydroxopentacyanonitrosylmolybdate(II), $K_4[Mo^{II}(OH)_2(CN)_5(NO)]$. This compound was first prepared, but wrongly formulated, by Hofmann;[4] later Nast and Gehring,[2] after extensive analyses, ascribed to it the formula $K_4[Mo^0(CN)_5NO],2H_2O$. We have examined the infrared spectra of this compound and those of some other hydroxycyano-complexes of molybdenum (Table 2). The main features of the spectrum of the compound are: (*a*) Strong absorption maxima in the region 3300—3500 cm.$^{-1}$, indicative of hydroxy-groups. Similar absorptions are found in the spectra of the other hydroxycyano-molybdenum complexes which, on other grounds, must be formulated as having hydroxy-groups bound to the metal atom. (*b*) In the region 2040—2200 cm.$^{-1}$ there is a rather complex splitting of cyanide group frequencies. The positions of the main peaks are comparable to those found for the hydroxycyano-complexes, but the degree of splitting is much greater. This can be attributed partly to the greater asymmetry introduced by the nitric oxide ligand and also to different crystalline lattice effects. (*c*) There is very weak and diffuse absorption at 1620 cm.$^{-1}$ which can be attributed to traces of water in the mulls. (*d*) At 1595 cm.$^{-1}$ there is an intense absorption which we assign as an N–O stretching frequency of the bound NO^+ group. Hieber and Jahn[5] have recently claimed that a peak at 1410 cm.$^{-1}$ should be assigned to the N–O stretching frequency. We have examined this region in both Nujol and hexachlorobutadiene mulls and consider that this very weak absorption is more likely to arise from a combination mode, especially because of its low intensity and the fact that absorption by an NO^+ group at such a low frequency is very unlikely (as suggested by experience with a large number of other nitric oxide complexes[6]). The frequency of the N–O stretching in this molybdenum compound and in the chromium compound discussed above is very low and occurs at the extreme end of the scale for NO^+ co-ordination.[3,6] The low value can in part be explained by the donation of electron density from the π-bonds of the nitric oxide group to the metal atom as suggested by Alderman and Owston[7] to explain the non-linearity of the M–N–O system in cobalt nitrosyl dithiocarbamate. (*e*) There are broad and strong peaks in the region 800—950 cm.$^{-1}$ which also occur in the hydroxycyano-compounds and in sodium, potassium, and lead molybdates (Table 2); these bands are not present in $K_3[Mo(CN)_8]$ or in $K_4[Mo(CN)_8]$ or in normal, sexaco-ordinate cyanonitrosyl-complexes.[3,6,8] It seems most likely that these absorptions are attributable to Mo–O stretching modes.

In addition to this spectral evidence, chemical and magnetic-susceptibility data also support the new formulation. Thus the complex does not lose water at 180° even under vacuum,[2] a fact we have confirmed. Magnetic-susceptibility measurements at room temperature show a slight paramagnetism ($\chi_g = +0{\cdot}36 \times 10^{-6}$ c.g.s.u.) which corresponds to considerably less than the moment for one unpaired spin. The complex is therefore diamagnetic, the first example, so far as we are aware, of such a state for Mo(II) in a dodecahedron. Recent theoretical work[9] indicates that octaco-ordinate Mo(II) complexes would be diamagnetic as the 4*d* orbitals are split into three singlets and a doublet level, under the influence of the ligand field for a dodecahedron arrangement.

The formulation of the nitrosyl as $K_4[Mo^{II}(OH)_2(CN)_5(NO)]$ suggested that other molybdenum species could be similarly reformulated. Thus the complex hydroxycyanide first prepared by von der Steide and Hofmann[4] was considered by Bucknall and Wardlaw[10] to be $K_3[Mo^{IV}(OH)_3(CN)_4H_2O],2H_2O$. We have studied its infrared spectrum

[4] von der Steide and Hofmann, *Z. anorg. Chem.*, 1896, **12**, 282.
[5] Hieber and Jahn, *Z. Naturforsch.*, 1958, **13**b, 196.
[6] Lewis, Irving, and Wilkinson, *J. Inorg. Nuclear Chem.*, 1958, **7**, 32.
[7] Alderman and Owston, *Nature*, 1956, **178**, 1071.
[8] Herington and Kynaston, *J.*, 1955, 3555.
[9] Griffiths, Owen, and Ward, *Proc. Roy. Soc.*, 1953, *A*, **219**, 526.
[10] Bucknall and Wardlaw, *J.*, 1927, 2981.

(Table 2) and found that its magnetic susceptibility corresponds to a moment of 1·91 B.M. It therefore appears that the complex is derived from Mo(v) and is best formulated as $K_3[Mo^V(OH)_4(CN)_4],2H_2O$. An alternative formulation of the hydroxy-complex species with Mo=O bonds, *e.g.*, $K_3[Mo^{III}O_2(CN)_4(H_2O)_2],2H_2O$, is also possible and would be consistent with the properties.

Experimental

Infrared measurements were made with a Perkin-Elmer Model 21 recording spectrophotometer with calcium fluoride, sodium chloride, and potassium bromide optics for the appropriate regions. The spectra were taken in Nujol or hexachlorobutadiene mulls. Magnetic measurements were made by the standard Gouy technique on finely ground solids. Polarograms were taken on a Tinsley recording instrument, Type 19/1.

Potassium Pentacyanonitrosylchromate(I) *Hydrate.*—Chromium trioxide (7 g.) was added to a cold saturated solution of potassium hydroxide (20 g.) with ice cooling. Saturated aqueous potassium cyanide (35 g.) was then added and the mixture filtered. Hydroxylamine hydrochloride (8 g.) was added to the filtrate and the solution was heated (steam-bath) for 2 hr., and then filtered and cooled, and the filtrate poured, with stirring, into ethanol (95%; 250 ml.). The precipitate was dissolved in the minimum quantity of water, and the compound again precipitated with ethanol; two crystallisations from water gave large bright green crystals (5 g., 20%) (Found: K, 33·6; Cr, 14·9; C, 18·05; N, 24·3; H_2O, 5·1. $K_3[Cr(CN)_5NO],H_2O$ requires K, 33·8; Cr, 15·0; C, 17·3; N, 24·2; H_2O, 5·2%).

The water of crystallisation was removed at 80° *in vacuo* to give the anhydrous complex.

Potassium Dihydroxypentacyanonitrosylmolybdate(II).—This was prepared by the literature method [2] (Found: K, 35·5; C, 13·1. Calc. for $K_4[Mo(OH)_2(CN)_5NO]$: K, 34·9; C, 13·45%). Potassium tetrahydroxotetracyanomolybdate(v) was obtained as described earlier [10] (Found: K, 27·3; Mo, 22·8. Calc. for $K_3[Mo(CN)_4(OH)_4],2H_2O$: K, 27·8; Mo, 22·7%). The complexes $K_4[Mo(CN)_4(OH)_4]$ [4,10,11] and $K_4[Mo(CN)_5(OH)_2]$ [12] were prepared by published methods.

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Inorganic Chemistry Laboratories,
Imperial College, London, S.W.7.
William Ramsay and Ralph Forster Laboratories,
University College, London, W.C.1.

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[11] Péchard, *Compt. rend.*, 1894, **118**, 804.
[12] Collenberg, *Z. anorg. Chem.*, 1924, **136**, 249.

XUM

180. *Vibrational Frequency Correlations in Heterocyclic Molecules. Part V.*[1] *The Infrared Spectra of Some Enolic Structures Related to Oxindole and Isatin.*

By D. G. O'Sullivan and P. W. Sadler.

Chemical properties and infrared spectra indicate that *N*-methyloxindole-3-aldehyde possesses a hydroxymethylene structure at position 3. This enolic form exists in the solid and in solution because of the formation of strong resonance-stabilised intramolecular hydrogen bonds of the type well known with aliphatic diketones.

Substituted 4 : 5 : 6 : 7-tetrahydro-*N*-phenylisatins also exist as the 3-enols, stabilised by (i) hydrogen bonding and (ii) extension of conjugation. The carbonyl frequencies respond to changes in the Hammett σ values of aromatic ring substituents in the usual way, the substituent effect being transmitted, although to a reduced extent, through the tertiary nitrogen atom. The substituent effect on the stretching frequencies of those carbonyl groups involved in hydrogen bonding is greater than on unbonded carbonyl groups. Comments are made on other features of the spectra of these compounds and their ethers, anils, and oximes.

The spectrum of indole-3-aldehyde indicates that its carbonyl group has a low bond order and suggests hydrogen-bonded association of a mainly dipolar character.

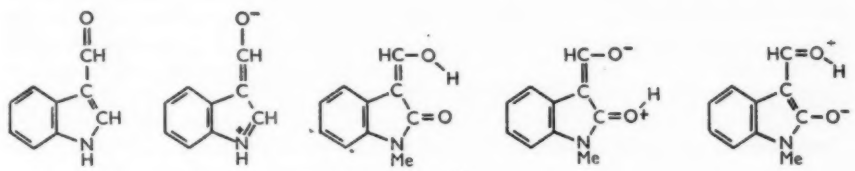
Summation of bond energies [2] shows that a simple keto-structure is more stable than the enol by about 18 kcal. mole^{-1} for ketones and 15 kcal. mole^{-1} for aldehydes, and an amide is more stable than the imino-alcohol by about 10 kcal. mole^{-1}. Many other factors can arise, particularly in cyclic systems, which may invalidate a simple application of these results. Nevertheless, of the large number of non-phenolic cyclic compounds which could exhibit these types of tautomerism and which have been studied,[3] most have been shown to exist in the ketonic form in the pure state and in solution. It is likely, however, that in solution the compounds exist in equilibrium with minute proportions of the enol. The small variation of $\Delta F(\equiv RT \ln\{[\text{keto}]/[\text{enol}]\})$ with change in the relative concentrations in solution implies that an energy difference of only 6 kcal. mole^{-1} between the two forms will raise the [keto]/[enol] ratio to over 99%, *i.e.*, the enol present will probably be undetectable. The solution may still, however, exhibit enolic reactions if (*a*) these reactions are rapid, (*b*) tautomeric equilibrium is rapidly attained, and (*c*) the keto-form is in itself inert towards the reagents. Where a substance readily undergoes both ketonic and enolic reactions, purely chemical evidence is probably inconclusive. These remarks apply also to amide–imidol tautomerism.

In compounds where enolic forms are favoured, such as phenols and β-diketones, additional features are recognised as exerting a dominant influence on the structure.[4] Thus carbonyl compounds exist almost exclusively in the keto-form unless features such as hydrogen bonding, steric hindrance, or the possible extension of conjugation stabilise the alternative form. After a brief treatment of indole-3-aldehyde, this paper deals with a spectroscopic study of two sets of cyclic compounds which possess chemical properties suggesting the preponderance of enolic tautomers.

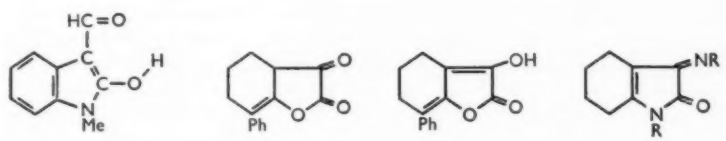
[1] Part IV, Holt, Kellie, O'Sullivan, and Sadler, *J.*, 1958, 1217.
[2] Branch and Calvin, "The Theory of Organic Chemistry," Prentice-Hall, New York, 1946.
[3] Culbertson, Decius, and Christensen, *J. Amer. Chem. Soc.*, 1952, **74**, 4834; Brown and Short, *J.*, 1953, **331**; Sensi and Gallo, *Ann. Chim.* (*Italy*), 1954, **44**, 232; Brown, Hoerger, and Mason, *J.*, 1955, 211; Gibson, Kynaston, and Lindsey, *ibid.*, p. 4340; O'Sullivan and Sadler, *J.*, 1956, 2202; Kellie, O'Sullivan, and Sadler, *J.*, 1957, 3809; Mason, *ibid.*, pp. 4874, 5010.
[4] Thomson, *Quart. Reviews*, 1956, **10**, 27.

Results and Discussion

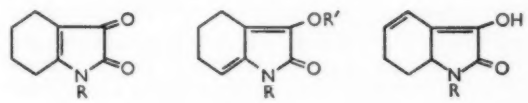
Indole-3-aldehyde.—In potassium bromide discs and in chloroform this compound shows an NH stretching frequency as a broad band between 3120 and 2900 cm.$^{-1}$. No band is present at a higher frequency. As indole possesses maxima between 3491 and 3447 cm.$^{-1}$ in various solvents, and only very weak maxima near 3340 cm.$^{-1}$ due to hydrogen-bonded association,[9] it is clear that the NH bond in indole-3-aldehyde is involved in fairly strong hydrogen bonding. The carbonyl stretching frequency occurring at 1631 cm.$^{-1}$ in the solid and 1655 cm.$^{-1}$ in chloroform suggests that this group possesses a low bond order. These results show that the dipolar form (II) makes a large contribution to the structure of indole-3-aldehyde and dipolar association occurs so that, in the solid, structures (I) and (II) are the main contributions to each unit in an extensive hydrogen-bonded polymer. Thus a definite aldehydic structure exists, but the carbonyl group possesses a much reduced bond order. The concomitant proximity of a hydrogen atom in the polymer enables the compound to possess enolic properties in addition to its aldehydic properties. Enolic properties result when the N–H bond is split, and the aldehydic properties when the H · · · O link is broken. The possible alternative that hydrogen bonding occurs between an aldehydic and an enolic molecule may be excluded on the following grounds: (*a*) the absence of



(I) (II) (III) (IV) (V)



(VI) (VII) (VIII) (IX)



(X) (XI) (XII)

a free, or very weakly associated, NH stretching frequency,[9] (*b*) the absence of a hydrogen-bonded OH stretching frequency, and (*c*) the very low value for the CO stretching frequency.[10]

[5] Van Order and Lindwall, *J. Org. Chem.*, 1945, **10**, 128.
[6] W. König, *J. pr. Chem.*, 1911, **84**, 194.
[7] Angeli and Marchetti, *Atti R. Accad. Lincei*, 1907, **16**, 381; Angeli and Allesandri, *ibid.*, 1914, **23**, 93.
[8] Sumpter and Miller, "Heterocyclic Compounds with Indole and Carbazole Systems," Interscience, New York, 1954, p. 42.
[9] Fuson, Josien, Powell, and Utterbach, *J. Chem. Phys.*, 1952, **20**, 145.
[10] Rasmussen, Tunnicliff, and Brattain, *J. Amer. Chem. Soc.*, 1949, **71**, 1068.

N-*Methyloxindole-3-aldehyde*.—Although oxindole-3-aldehyde and its 1-methyl derivative form typical carbonylic derivatives (*e.g.*, oximes,[11] semicarbazones,[12] and aldimines [13]), yet the ferric chloride test for OH is positive and acetyl, benzoyl, and benzenesulphonyl derivatives are readily formed.[12,14] Under different conditions a variety of methyl

TABLE 1. *Frequencies in spectra of compounds in potassium bromide discs.*

Compound	4000—1425 cm.$^{-1}$ region							
A, Indole-3-aldehyde	3120s†	2900s†	1631s		1615w	1577w	1519m 1498m	1445s
B, Indole-3-aldoxime	3400—2700s†			1641s			1508w 1493w	1462s
C, 1-Methyloxindole-3-aldehyde	3100—2850m† 2600—2400s†		1680s	1633s	1611s	1555m	1470s	
D, 1-Methyloxindole-3-aldoxime	3400m	2905m	1696m	1646m	1611s	1577s	1492m 1474m	1437m
E, Isatin α-oxime	3400—3000 m†		1716m	1641m	1614s		1483m	1466m
F, Isatin β-oxime	3200—2600s†		1712s	1662m	1621s			1465s
4 : 5 : 6 : 7-*Tetrahydroisatins*								
G, 1-Phenyl-	3210s	2910s	1670s	1650s	1596m		1503s	1451w 1433w
H, 1-(*m*-Chlorophenyl)-	3170s	2900w	1669s	1652s	1595m		1522w 1484m	1433m
I, Methyl ether* of 1-phenyl-		2915w	1705s	1652m 1639s	1599m		1499s	1460m 1434m
J, *m*-Chloroanil* of 1-(*m*-chlorophenyl)-			1688s	1640s	1598s	1579s	1525s 1483s	1432s
K, Oxime* of 1-phenyl-	3300s	2915w	1705s	1646w	1600m		1518s	1447s
L, 1-Benzyl-	3225s	2920w	1678s	1660s	1590w		1501w	1448m 1430m
M, Oxime* of 1-benzyl-	3300s	2915m	1674s	1659s			1528w 1498w	1458m

Compound	1425—900 cm.$^{-1}$ region											
A,	1394s	1338m	1300m	1248s		1152m	1127s	1086m		1008w		
B,	1418s	1343s		1238s			1133s	1099s		1009w		930s 906m
C,	1381s	1344w	1276m	1233s	1190m	1164w	1123s	1110s		1027w		928w
D,	1390m	1348m	1270m	1240m		1149w	1128m	1094s 1073w	1044m	985w		910w
E,		1329m		1225w		1144w				1027w		930m
F,	1391w	1349s	1301w	1220m	1195m			1100w	1030s			940w
G,	1409s	1341w	1313s	1247s	1191m	1168m		1071w	1050w	983m	966w	
H,	1408s	1311s	1300m	1248m	1186m	1169m		1073w	1047w	1002w 986m		
I,	1409s 1376m	1336m	1291s	1260w 1248s	1194s 1178m	1160s	1123m	1076w	1054w	1020s 989m	946w	
J,	1408s	1345w 1328m	1285w 1273w	1260w 1230w	1178m	1154w		1088w 1073w	1051w	997w	958w	928w
K,		1318m		1240w	1196s			1073w	1059w 1039w	990w	958w	941w 906w
L,	1410s	1368m 1352m	1342m 1316s	1239m	1198w 1179w	1151w	1137w	1081w	1058w 1035w	1019m 968m		935w
M,	1401s	1366m	1287w	1233w		1141w	1119w	1091w		1028m	950s	928w 913w

* At position 3. † Broad band.

derivatives may be obtained.[14,15] In the present study the 1-methyl compound [16] has been selected for scrutiny to avoid the possibility of tautomerism involving the NH group. Spectral features are given in Table 1.

[11] Friedlander and Kielbasinski, *Ber.*, 1911, **44**, 3098.
[12] Fischer and Smeykal, *Ber.*, 1923, **56**, 2368.
[13] Kalb and Berrer, *Ber.*, 1924, **57**, 2105.
[14] Horner, *Annalen*, 1941, **548**, 117; Gränacher and Mahal, *Helv. Chim. Acta*, 1923, **6**, 467.
[15] Julian, Pikl, and Boggess, *J. Amer. Chem. Soc.*, 1934, **56**, 1797.
[16] Julian, Meyer, and Printy in " Heterocyclic Compounds " (ed. Elderfield), John Wiley, New York, 1952, Vol. III, p. 153.

Absence of any absorption above 3100 cm.$^{-1}$ either in the solid or in solution in chloroform or carbon tetrachloride shows the absence of a free OH group, but the broad band of considerable intensity between 2600 and 2400 cm.$^{-1}$ shows the presence of very strong hydrogen bonding which is only explicable on the assumption that resonance-stabilised intramolecular hydrogen bonding, as found in aliphatic β-diketones and β-keto-esters,[10,17] is present. The unperturbed forms of this conjugated chelate compound are represented by structures (III)—(VI). As the molecule is not a symmetrical diketone, an unequal contribution is to be expected from structures of type (III) and (VI), but it is likely that all four structures make a substantial contribution to the resonance system, as undue predominance of one form would weaken the hydrogen bonding and would not therefore produce the band at 2600—2400 cm.$^{-1}$. Bands at 1680 cm.$^{-1}$ and 1633 cm.$^{-1}$ are produced essentially by stretching vibrations of C=O and C=C bonds, but vibrational interactions may occur in this system and distinct assignments may not be possible.

The oxime exhibits an OH stretching frequency at 3400 cm.$^{-1}$ and a carbonyl frequency at 1696 cm.$^{-1}$, both of which are unchanged in solution. It therefore possesses the expected structure but has a much weaker intramolecular hydrogen bond than the parent compound. Considerable similarity exists between the spectrum of 1-methyloxindole-3-aldoxime and 1-methylisatin β-oxime, and this similarity also extends to isatin β-oxime itself (Table 1). The skeletons are undoubtedly the same and provisional assignments of the aldoxime frequencies at 1240 and 1044 cm.$^{-1}$ to N–O–H bending and N–OH stretching modes are possible. Table 1 shows that very marked differences exist between the spectra of these compounds and that of isatin α-oxime.

Reduced Isatins.—Condensation of 2-phenyl*cyclo*hexanone with dimethyl oxalate gives a lactone [18] which has been shown unequivocally to have structure (VII) or (VIII). The very pronounced enolic properties and the clearly enhanced conjugation make it likely that (VIII) is the structure adopted in most circumstances. *cyclo*Hexanone itself condenses with dimethyl oxalate to give a substituted glyoxylic ester which reacts with amines to form anils of structure (IX).[19] Acid hydrolysis of the anils produces *N*-substituted 4 : 5 : 6 : 7-tetrahydroisatins which, Horwitz [19] suggests, consist of tautomeric mixtures of keto- and enol forms. Although phenylhydrazones are formed at position 3 and condensations occur with *o*-phenylenediamine to give quinoxalines, the compounds readily undergo methylation at the 3-position, and form other enolic derivatives with equal ease. Formulae (X) and (XI; R′ = H) represent the most probable structures for these compounds, (XII) being the only other possibility. Two hydrogen atoms would have to migrate to different positions in structure (XII) to produce ketonic functions at position 3. Therefore, this structure is most unlikely. The existence of lactones (VIII) shows that the type of conjugated ring system in structure (XI) is stable and the close analogy in the reactivities of the two sets of compounds [18,19] strongly suggests the presence of similar ring systems. Also, if R is a substituted phenyl group, more extensive conjugation is possible in (XI) than in (XII). Infrared studies were designed to discover which structure was adopted in the solid and in non-polar solvents and to study the extent to which substituent effects could be transmitted in this system.

Structure (X), possessing no OH or NH bonds, should show no absorption at wavelengths greater than 2000 cm.$^{-1}$ except for CH stretching frequencies near 3000—2900 cm.$^{-1}$ and possibly for weak overtone frequencies, the strongest of which should be the first carbonyl stretching harmonic near 3400 cm.$^{-1}$. Table 1 shows that a strong and, for this region in the spectrum, very sharp band is present at 3210 cm.$^{-1}$ in the solid, which can only be a hydrogen-bonded OH stretching frequency. This maximum becomes a much broader absorption at about the same frequency in chloroform, whilst in carbon tetrachloride two sharp bands appear, one near 3490 cm.$^{-1}$ and the second near 3200 cm.$^{-1}$. These bands

[17] Rasmussen and Brattain, *J. Amer. Chem. Soc.*, 1949, **71**, 1073; Hunsberger, *ibid.*, 1950, **72**, 5626.
[18] Bachmann, Fujimoto, and Wick, *ibid.*, p. 1995.
[19] Horwitz, *ibid.*, 1953, **75**, 4060.

are present with all the substituted tetrahydro-*N*-phenylisatins but are completely absent from the spectra of the anils (IX) and the methyl ethers (XI; R′ = Me), neither of which can contain hydroxyl groups. The bands near 3200 cm.$^{-1}$ are produced by simple hydrogen bonding of reasonable strength and undoubtedly arise from C=O · · · HO linkages which might be of inter- or intra-molecular type. The high m. p.s of the reduced isatins compared with those of their methyl ethers suggest that intermolecular hydrogen-bonded dimers exist in the solid, whilst the broad absorption in chloroform suggests the presence of both dimer and monomer. The sharper absorption peak occurring between 3200 and 3180 cm.$^{-1}$ in carbon tetrachloride is probably produced by OH groups engaged in intra-molecular bonding. The sharp maximum near 3490 cm.$^{-1}$ in carbon tetrachloride could be due to OH groups involved in weak hydrogen bonding [17] when such dimers as exist would be formed by hydroxyl association, leaving free ketone groups in the 2-positions. Alternatively, dimers could possess CO · · · HO bonds of such reduced strength that the CO groups are virtually unaffected and the OH frequencies only slightly depressed. Carbonyl stretching frequencies fully support these suggestions. The only absorption shown by the methyl ethers is a weak CH stretching frequency near 2915 cm.$^{-1}$. With the anils even this absorption is very weak indeed.

Carbonyl Frequencies.—The methyl ethers, each of which contains one carbonyl group which cannot be involved in hydrogen bonding, possess sharp maxima at about the same frequency both in the solid and in carbon tetrachloride (Table 2). This also applies to the anils (Table 2) but the molecular environment of the carbonyl group in the anils is very different from that in the ethers. Extended conjugation of the carbonyl group in the anils results in a lowering of its frequency. The reduced isatins themselves possess single carbonyl stretching frequencies in the solid and in chloroform. Their spectra at frequencies above 3000 cm.$^{-1}$ suggest that these are stretching frequencies of carbonyl groups involved in hydrogen bonding, and this is strongly supported by the carbonyl frequencies in carbon tetrachloride. Two carbonyl maxima are given in this solvent (Table 2), one slightly above the frequency for the corresponding methyl ether and the other at a frequency slightly above the chloroform maximum. An equilibrium clearly exists, in carbon tetrachloride, between molecules in which the carbonyl group is either unbonded or very weakly bonded and those in which it is involved in quite strong hydrogen bonding. An alternative possibility, that the two frequencies arise from the existence of at least some of the 3-oxo-form, may be discounted from the position of these frequencies, the presence and position of the two OH stretching frequencies, and from the way in which the frequencies vary with the character and position of benzene ring substituents. Thus one concludes that, in the solid, the compound exists as an enol with the OH group fairly strongly hydrogen bonded to the carbonyl group of the adjacent molecule to form a dimer linked by two CO · · · HO bonds. In chloroform the main solute components are probably a mixture of monomer and dimer, the former possessing intra- and the latter inter-molecular CO · · · HO bonds of about equal strengths, whilst in carbon tetrachloride the main components are dimers possessing either OH · · · OH bonds and free carbonyl groups or very weak CO · · · HO bonds and monomers containing intramolecular CO · · · HO bonds.*

Substituent Effects on Carbonyl Frequencies.—(a) *Methyl ethers.* Seven of these derivatives of tetrahydro-1-phenylisatin, possessing benzene-ring substituents with Hammett σ values [20] lying over a range of nearly one unit, were examined spectroscopically. Table 2 shows that substituents exert an effect on the carbonyl stretching frequencies ν in carbon tetrachloride. As usual, the relation between ν and σ is linear, the equation of the regression line for ν being $\nu = 1702{\cdot}9 + 6{\cdot}04\sigma$, and the correlation coefficient r is 0·980. The substituent effect clearly gets transmitted through the nitrogen atom, but comparison with other compounds shows that it is reduced in magnitude by approximately 50%.

* The views expressed in this and the preceding paragraph have been modified to take account of a criticism kindly made by a Referee.

[20] Hammett, "Physical Organic Chemistry," McGraw-Hill, New York, 1940, p. 188; Jaffé, *Chem. Rev.*, 1953, **53**, 191.

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(b) *Enols.* The upper carbonyl stretching frequency shown by the enols in carbon tetrachloride is not only near that of their methyl ethers, but substituents have quantitatively about the same effect on both these sets of frequencies. This confirms that the carbonyl frequency in the enols is produced by the α-carbonyl group not markedly affected by hydrogen bonding. The equation of the regression line for the frequencies is $\nu = 1709{\cdot}4 + 6{\cdot}16\sigma$ and the correlation coefficient is 0·963.

The lower carbonyl stretching frequency in carbon tetrachloride is probably produced by the α-carbonyl group involved in intramolecular hydrogen bonding. Frequencies increase in a linear fashion with the σ values of substituents, the effect being about twice the effect on the upper frequencies. The regression line for the ν values is $\nu = 1689{\cdot}3 + 14{\cdot}17\sigma$ and the correlation coefficient is 0·936. Frequencies of the carbonyl band in chloroform lie slightly below those in carbon tetrachloride and also arise from hydrogen-bonded carbonyl groups. Here the regression line for the frequencies is $\nu = 1683{\cdot}9 + 17{\cdot}83\sigma$, and the correlation coefficient 0·963. Where the maxima in chloroform cover a range of values, the central frequency is recorded in Table 2 and is used in computing the regression line and correlation coefficient. Solid-state infrared spectra are similar to those in chloroform. It is clear from Table 3 that in all these cases substituent effects are greater on a strongly

TABLE 2. *Carbonyl stretching frequencies of substituted 4 : 5 : 6 : 7-tetrahydro-1-phenylisatins and related compounds.*

		Frequencies (cm.$^{-1}$) of compounds				
		Enol in	Enol in CCl_4		Methyl ether	Anil in
Subst.	σ Value	$CHCl_3$	Band II	Band I	in CCl_4	$CHCl_3$
p-NMe_2	−0·6	—	—	—	—	1677
p-MeO	−0·268	1678 *	1685 *	1708	1701	1682 *
p-Me	−0·170	1683 *	1690	1709	1702	1682
m-Me	−0·069	—	—	—	—	1684
None	0·0	1684	1689	1709	1703	—
m-MeO	0·115	1684	1689	1709	1703	1686
p-Cl	0·227	1687	1691	1711	1705	1688
m-Cl	0·373	1693	1694	1712	1705	1690
m-NO_2	0·710	1696	1701	1714	1707	1695

* Central frequency is quoted for a maximum extending over about 4 cm.$^{-1}$. Where blanks occur in these columns the frequencies have not been measured. All bands quoted are intense.

TABLE 3. *Effect of hydrogen bonding, involving the carbonyl group, on the slope* $d\nu(CO)/d\sigma$ *for substituted 4 : 5 : 6 : 7-tetrahydro-1-phenylisatins and substituted benzoic acids.*

		Carbonyl stretching frequencies (cm.$^{-1}$)				
Subst.	σ Value	Enol in CCl_4 Band I	BzOH in CCl_4 * (monomer)	Enol in CCl_4 Band II	BzOH in MeOH * (monomer)	BzOH in CCl_4 * (dimer)
p-NH_2 ...	−0·660	—	—	—	1690	—
p-MeO ...	−0·268	1709	1737	1685	1695	1691
p-Me ...	−0·170	1709	1739	1690	1700	1693
None ...	0·0	1709	1743	1689	1705	1693
m-MeO	0·115	1709	—	1689	—	—
p-Br ...	0·232	—	—	—	1710	—
p-Cl	0·227	1711	1746	1691	1713	1699
m-Cl ...	0·373	1712	1746	1694	1715	1701
m-NO_2 ...	0·710	1714	1750	1701	1723	1705

* Estimates of the accuracy of these frequency measurements varying from ±1 to ±5 cm.$^{-1}$ have also been reported.[22]

hydrogen-bonded carbonyl group than on a free group or on one involved in very weak hydrogen bonding. Other examples have been noted of a larger substituent effect on groups involved in hydrogen bonding than on similar unbonded groups (cf., *e.g.*, acetanilide with acetophenone or benzophenone [21]). A striking example is also evident in the values given

[21] O'Sullivan and Sadler, *J. Org. Chem.*, 1956, **21**, 1179.
[22] Flett, *Trans. Faraday Soc.*, 1948, **44**, 767.

by Flett [22] of the effect of substituents on the carbonyl frequencies of carboxylic acids in carbon tetrachloride and methanol.

Change of solvent from carbon tetrachloride to methanol produces the following two effects on the carbonyl frequencies of benzoic acid monomers: (i) all frequencies are reduced, showing that hydrogen-bonded association occurs between the carbonyl group and methanol, and (ii) the displacement of frequencies by substituents is notably enhanced, strongly suggesting that the substituent effect is greater in carbonyl groups involved in this type of hydrogen bonding. This is, however, a matter of some complexity, as smaller substituent effects are exerted on the very strongly hydrogen-bonded carbonyl group of

TABLE 4. *σ Values and some lower-frequency bands of substituted 4 : 5 : 6 : 7-tetrahydro-1-phenylisatins in potassium bromide discs.*

Subst.	σ Value	Frequencies ($cm.^{-1}$)				
p-Me	−0·170	1613	1518	1409	1193	686
None	0·0	1596	1503	1409	1191	692
p-Cl	0·227	1595w	1497	1414	1186	693w
m-Cl	0·373	1595	1484	1410	1186	719
m-NO_2	0·710	1586w	1484	1418	1180	727

Bands are of medium or high intensity apart from the exceptions noted in the Table.

the benzoic acid dimer. The symmetry of the dimer molecules does not, in itself, account for the observed phenomena. Although the bond order of the carbonyl group in the dimer is lower than in the hydrogen-bonded monomer, equal contributions of the two principal unperturbed structures result in less polarisation of the carbonyl group than is present in the associated monomer.

A linear correlation also exists between the carbonyl frequencies of the anils and the σ values of their substituents. The regression line for the frequencies is $\nu = 1685{\cdot}0 + 13{\cdot}60\sigma$ and the correlation coefficient is 0·997. Here the large displacements are produced by the sum of two components, the effect transmitted through the tertiary nitrogen atom as in the methyl ethers, and an additional effect arising from the substituent in the second benzene ring and being transmitted through the N=C linkage. As hydrogen bonding cannot occur in these molecules no complications can arise from this cause. Consequently, it can be assumed that substituent effects on carbonyl frequencies are readily transmitted through an N=C linkage. However, the differences in structure between the methyl ether or enol and the anil prevent any quantitative assessment of the transmissive power of this group in the anils. These studies clearly show that hydrogen bonding can confuse the study, by infrared spectra, of the ability of groupings to transmit substituent effects, and imply that such comparative studies should involve parallel series of compounds in which hydrogen bonding cannot occur and should, as far as possible, utilise non-polar solvents.

Lower Frequencies of Reduced Isatins and Their Derivatives.—Direct evidence for the existence of a cyclic conjugated diene-ketonic system is not readily disentangled. Carbonyl frequencies of conjugated carbonyls in six-membered rings lie in the 1680—1660 $cm.^{-1}$ region.[23] If the carbonyl group is exocyclic to a five-membered ring [24] this frequency range is raised by about 30 $cm.^{-1}$ to the higher carbonyl frequencies of the reduced isatins. Thus the magnitudes of the carbonyl frequencies themselves are consistent with the proposed structures.

Analysis of ethylenic frequencies of conjugated systems in some cases provides information on the structural and stereochemical arrangement of the double bonds.[23,25] Un-

[23] Blout, Fields, and Karplus, *J. Amer. Chem. Soc.*, 1948, **70**, 194; Jones, Humphries, and Dobriner, *ibid.*, 1949, **71**, 241.

[24] Förster, *Z. phys. Chem.*, 1939, **43**, *B*, 58; Coulson and Moffit, *Phil. Mag.*, 1949, **40**, 1; Bladon, Fabian, Henbest, Koch, and Wood, *J.*, 1951, 2402; O'Sullivan and Sadler, *J.*, 1957, 2916.

[25] Rasmussen and Brattain, *J. Chem. Phys.*, 1947, **15**, 120; Jones, Humphries, Packard, and Dobriner, *J. Amer. Chem. Soc.*, 1950, **72**, 86; Freeman, *ibid.*, 1953, **75**, 1859; Lunde and Zechmeister, *ibid.*, 1955, **77**, 1647; Sheppard and Simpson, *Quart. Reviews*, 1952, **6**, 1; Henbest, Meakins, and Wood, *J.*, 1954, 800; Allan, Meakins, and Whiting, *J.*, 1955, 1874; Henbest, Meakins, Nicholls, and Wilson, *J.*, 1957, 997.

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fortunately, no known structures sufficiently similar to the present ones have been examined. Consequently, these frequencies cannot be used to confirm structure (XI), or to unravel a stereochemical pattern. However, a number of general comments are possible on the lower frequencies. Apart from the methyl symmetrical bending and methyl rocking frequencies at 1376 and 1178 cm.$^{-1}$ respectively, the C–O–C asymmetrical and symmetrical stretching frequencies at 1123 and 1020 cm.$^{-1}$, and an unexplained additional C=C stretching frequency at 1639 cm.$^{-1}$, great similarity exists between the spectra of the methyl ethers and enols. Support that this gives to the evidence that these possess similar structures is weakened, however, because both the anils and the oximes possess many spectral features in common with the ethers and enols.

Bands near 1650, 1600, and 1500 cm.$^{-1}$ are C=C stretching frequencies arising partly in the unsaturated and partly in the aromatic ring systems. Aromatic ring CH bonding frequencies occur near 770 cm.$^{-1}$ and bands characteristic of different types of benzene-ring substitution patterns occur between 880 and 780 cm.$^{-1}$ in the substituted reduced isatins.

Out-of-plane ethylenic CH deformation probably gives rise to the medium-intensity band near 990 cm.$^{-1}$ in the substituted tetrahydroisatins and in their methyl ethers. The band present at 997 cm.$^{-1}$ in the anil (Table 1), which cannot of course be an ethylenic CH frequency, is of much lower intensity. The band that occurs between 1460 and 1430 cm.$^{-1}$ in all the reduced isatins and their methyl ethers arises from CH_2 deformations in the reduced ring,[26] and the band near 1410 cm.$^{-1}$ might also arise from this cause as conjugation with carbonyl groups can produce a depression of this magnitude.[27]

Table 4 provides evidence of variation of some lower frequencies with the σ values of substituents. Thus the bands near 1600, 1500, and 1190 cm.$^{-1}$ possess frequencies that decrease with increase of σ values and the frequencies of bands near 1415 and 700 cm.$^{-1}$ increase with σ values. Only a few compounds have been included and disc spectra are not as reliable as solution spectra, but the possible existence of these correlations supports the premise that considerable conjugation exists throughout the system. Thus, to a limited extent, the lower frequencies support the enolic character of the reduced isatins and the stabilisation of the enol form by hydrogen bonding and extension of conjugation. It has been proved in at least two cases [28] that steric factors can stabilise enolic forms, and it is conceivable that the stabilities of the reduced ring systems may be a significant factor in this case also.

Spectra of the oximes (Table 1) are similar to those of the reduced isatins and do not include certain characteristic features of the spectra of isatin β-oximes,[29] such as the very intense band near 1020 cm.$^{-1}$.

Experimental

Spectra.—Compounds were examined under identical conditions for each medium. The instrument used was a Perkin–Elmer 21 double-beam recording spectrometer fitted with a rock-salt prism.

1-*Methyloxindole-3-aldehyde.*—Prepared by the method of Friedlander and Kielbasinski,[11] this compound formed yellow plates, m. p. 186°. Its oxime [11] formed deep red plates, m. p. 203°.

1-*Aryl*-4 : 5 : 6 : 7-*tetrahydroisatin* 3-*Imines* (IX) (see Table 5).—Ethyl 2-oxo*cyclo*hexylglyoxylate (0·5 mol.) and the substituted aromatic amine (2 mol.) were heated in methanol under reflux for 3 hr. After cooling, the product was filtered off and washed with methanol. Further material was obtained by adding water to the filtrate, cooling, and then allowing the liquor to crystallise. With *m*-nitroaniline, heating was with propan-2-ol and for 12 hr.

The unsubstituted compound and the *p*-methoxy- and the *p*-chloro-compound were purified by crystallisation from methanol, the *m*-nitro-compound from *n*-butanol, and the remaining compounds of this class from ethanol.

[26] Jones and Cole, *J. Amer. Chem. Soc.*, 1952, **74**, 5648; Jones, Cole, and Nolin, *ibid.*, p. 5662.
[27] Francis, *J. Chem. Phys.*, 1951, **19**, 942.
[28] Fuson, Corse, and McKeever, *J. Amer. Chem. Soc.*, 1940, **62**, 3250; Kohler, Tishler, and Potter, *ibid.*, 1935, **57**, 2517.
[29] O'Sullivan and Sadler, *J. Org. Chem.*, 1957, **22**, 283.

1-*Aryl*-4 : 5 : 6 : 7-*tetrahydroisatins* (XI; R′ = H) (see Table 5, ii).—The anil (8 g.) was suspended in a mixture of propan-2-ol (60 ml.) and concentrated hydrochloric acid (25 ml.) and heated under reflux for 3 hr. After concentration of the product *in vacuo*, the residue was crystallised from aqueous ethanol except for the *m*-methoxy- and the *m*-nitro-compound. With

TABLE 5. *Reduced isatins and derivatives.*

Subst. R	M. p.	Appearance	Yield (%)	Found (%) C	Found (%) H	Formula	Required (%) C	Required (%) H
(i) *Imines* (IX)								
Phenyl-[19]	193°	Yellow prisms	58	—	—	—	—	
p-*Tolyl-*	211	Yellow prisms	71	80·0	6·8	$C_{22}H_{22}ON_2$	80·0	6·7
m-*Tolyl-*	160	Pale yellow plates	38	79·8	6·8	$C_{22}H_{22}ON_2$	80·0	6·7
p-*Methoxyphenyl-*	173	Yellow plates	60	73·3	6·1	$C_{22}H_{22}O_2N_2$	72·9	6·1
m-*Methoxyphenyl-*	148	Pale yellow plates	51	72·9	6·5	$C_{22}H_{22}O_2N_2$	72·9	6·1
p-*Chlorophenyl-* ...	200	Pale yellow needles	46	64·4	4·4	$C_{20}H_{16}ON_2Cl_2$	64·7	4·3
m-*Chlorophenyl-* ...	171	Pale yellow needles	64	64·4	4·3	$C_{20}H_{16}ON_2Cl_2$	64·7	4·3
m-*Nitrophenyl-* ...	219	Deep yellow needles	69	61·3	4·1	$C_{20}H_{16}O_5N_4$	61·2	4·1
p-*Dimethylamino-phenyl-*	263	Bronze needles	35	73·9	7·0	$C_{24}H_{28}ON_4$	74·2	7·2
Benzyl-[19]	123	White needles	63	—	—	—	—	—
(ii) *Reduced isatins* (XI; R′ = H).								
Phenyl-[19]	186°	Pale yellow prisms	60	—	—	—	—	
p-Tolyl-[19]	195	White prisms	66	—	—	—	—	—
p-*Methoxyphenyl-*	211	White needles	57	70·2	6·0	$C_{15}H_{15}O_3N$	70·0	5·8
m-*Methoxyphenyl-*	145	Cream plates	47	70·2	5·9	$C_{15}H_{15}O_3N$	70·0	5·8
p-*Chlorophenyl-* ...	184	White plates	63	64·0	4·7	$C_{14}H_{12}O_2NCl$	64·2	4·6
m-*Chlorophenyl-* ...	159	Buff needles	20	63·8	4·8	$C_{14}H_{12}O_2NCl$	64·2	4·6
m-*Nitrophenyl-* ...	188	Yellow needles	40	61·7	4·0	$C_{14}H_{12}O_4N_2$	61·8	4·4
Benzyl-[19]	172	White needles	60	—	—	—	—	—
(iii) 3-*Methoxy-compounds* (XI; R′ = Me)								
Phenyl-[19]	86°	Yellow needles	—	—	—	—	—	—
p-*Tolyl-*[19]	87	Yellow plates	—	75·6	6·5	$C_{16}H_{17}O_3N$	75·3	6·7
p-*Methoxyphenyl-*	110	Cream plates	—	70·6	6·3	$C_{16}H_{17}O_3N$	70·9	6·3
m-*Methoxyphenyl-*	—	Oil	—	70·6	6·2	$C_{16}H_{17}O_3N$	70·9	6·3
p-*Chlorophenyl-* ...	—	Oil	—	65·7	5·1	$C_{15}H_{14}O_2NCl$	65·4	5·1
m-*Chlorophenyl-* ...	168	White needles	—	65·2	5·0	$C_{15}H_{14}O_2NCl$	65·4	5·1
m-*Nitrophenyl-* ...	80	Yellow plates	—	63·3	4·7	$C_{15}H_{14}O_4N_2$	63·0	4·9

the former, the residue was extracted with boiling light petroleum (b. p. 100—120°) and the extracts were concentrated; the product that separated was recrystallised from light petroleum. The *m*-nitro-compound (8 g.) was heated under reflux for 6 hr. with *n*-butanol (60 ml.) and concentrated hydrochloric acid (25 ml.). After concentration of the product under reduced pressure, the solid was crystallised from aqueous methanol.

3-*Methoxy-derivatives* (XI; R′ = Me) (see Table 5, iii).—Diazomethane in ether was added to the tetrahydroisatin in the minimum quantity of acetone at 0°. The mixture was kept at 0° for 3 hr. and then at room temperature overnight. Excess of diazomethane was removed by distillation, and the residue was concentrated to a small volume and then allowed to evaporate to dryness at room temperature. The residual oil was crystallised from light petroleum (b. p. 40—60°).

Oximes of Reduced Isatins.—These were obtained from the parent compounds in the usual way and, after drying at 110°, they were found by analysis to be monohydrates. **4 : 5 : 6 : 7-*Tetrahydro*-1-*phenylisatin* 3-*oxime*** was obtained as pale yellow needles, m. p. 144° (Found: C, 64·7; H, 6·2. $C_{14}H_{16}O_3N_2$ requires C, 64·6; H, 6·2%). **1-*Benzyl*-4 : 5 : 6 : 7-*tetrahydroisatin* 3-*oxime*** formed yellow needles, m. p. 175° (Found: C, 65·5; H, 6·5. $C_{15}H_{18}O_3N_2$ requires C, 65·7; H, 6·6%).

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COURTAULD INSTITUTE OF BIOCHEMISTRY,
MIDDLESEX HOSPITAL MEDICAL SCHOOL,
LONDON, W.1.

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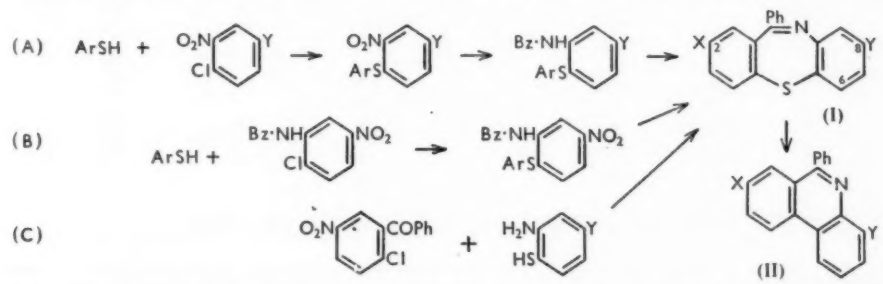
181. *Extrusion of Sulphur. Part IV.* Effect of Substituents in 11-Phenyldibenzo*[b,f]*-1 : 4-thiazepine.*

By R. H. B. Galt and J. D. Loudon.

11-Phenyldibenzo[*b,f*]-1 : 4-thiazepines variously substituted in the 2- and/or 8-position are synthesised and the effects of these substituents on extrusion of sulphur are examined.

In Part III * it was shown that 11-phenyldibenzo[*b,f*]-1 : 4-thiazepine (I; X = Y = H) is convertible into 9-phenylphenanthridine (II; X = Y = H) in high yield. Derivatives of the thiazepine are preparable in some variety by syntheses (A),[1] (B),[2] and (C),[3] thus providing an opportunity to examine the effect of substituents on extrusion of sulphur from this type of compound. Since substitution *para* to the sulphur atom is likely to be the most significant and free from steric complications, attention here is restricted to compounds of the general formula (I). Table 1 shows the range and sources of the



thiazepines examined, and Table 2 contains their percentage conversions into corresponding phenanthridines by standardised treatment with copper in quinoline (b. p. 238°) and in diethyl phthalate (b. p. 296°).

Table 1. 11-*Phenyldibenzo*[b,f]-1 : 4-*thiazepines* (I).

	Subst.		Method/			Found (%)			Required (%)		
(I)	X	Y	Source	M. p.	Formula	C	H	N	C	H	N
a	H	H	A	118°[1]	$C_{19}H_{13}NS$	—	—	—	—	—	—
b	H	Cl	A	150	$C_{19}H_{12}NClS$	71·1	4·0	4·3	70·9	3·7	4·4
c	Cl	H	A	134	〃	71·2	3·5	4·6	〃	〃	〃
d	H	Me	A	127	$C_{20}H_{15}NS$	79·8	4·6	4·5	79·7	5·0	4·6
e	Me	H	A	164	〃	79·6	4·7	4·6	〃	〃	〃
f	H	MeO	A	159	$C_{20}H_{15}ONS$	75·4	4·6	4·0	75·7	4·8	4·4
g	MeO	H	A	140	〃	75·8	4·9	4·5	〃	〃	〃
h	H	HO	If	255	$C_{19}H_{13}ONS$	75·2	4·1	—	75·2	4·3	—
i	HO	H	Ig	304	〃	75·1	4·4	—	〃	〃	—
j	H	NO_2	B	187	$C_{19}H_{12}O_2N_2S$	68·5	3·8	8·6	68·7	3·6	8·4
k	NO_2	H	C	159[3]	〃	—	—	—	—	—	—
l	Cl	Cl	A	152	$C_{19}H_{11}NCl_2S$	64·3	3·4	4·0	64·0	3·1	3·9
m	Me	Cl	A	147	$C_{20}H_{14}NClS$	71·5	4·2	4·2	71·5	4·2	4·2
n	Me	NO_2	B	185	$C_{20}H_{14}O_2N_2S$	69·2	3·8	8·0	69·4	4·1	8·1
o	NO_2	Me	C	177	〃	69·5	4·2	8·1	〃	〃	〃
p	MeO	NO_2	B	138	$C_{20}H_{14}O_3N_2S$	66·5	3·9	7·8	66·3	3·9	7·7

Although the conversion figures shown in Table 2 are usually repeatable within narrow limits they must be regarded as qualitative because accurate temperature control was difficult and the ranging properties of the products introduced unequal errors during

* Part III, *J.*, 1958, 1588.

[1] Brodrick, Nicholson, and Short, *J.*, 1954, 3857.
[2] This paper.
[3] Jarrett and Loudon, Part II, *J.*, 1957, 3818.

isolation. For instance, as control experiments showed, the phenanthridine may usually be separated from the reaction mixture by precipitation as the picrate, but this is slow and incomplete for 7-hydroxy-9-phenylphenanthridine or when a nitro-substituent is present: in these cases modified procedures were necessary (see Experimental section). The hydroxythiazepines (Ih) and Ii) were also the most sensitive of the compounds examined, and particularly with the latter isomer the incidence of side-reactions was apparent from the unusual deepening of colour during conversion.

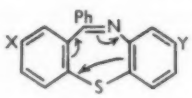
The highest yields recorded in Table 2 are not necessarily the best attainable but

TABLE 2. *Conversion* (%) *of thiazepines* (I) *into phenanthridines* (II).

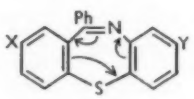
			240°	300°		
I	X	Y	60 min.	10 min.	15 min.	30 min.
a	H	H	Nil	57	73	86
b	H	Cl	—	61	73	81
c	Cl	H	—	56	71	84
d	H	Me	38	80	85	86
e	Me	H	—	51	—	83
f	H	MeO	79	82	—	82
g	MeO	H	10	77	85	88
h	H	HO	76	75	—	—
i	HO	H	Nil	(52)	—	—
j	H	NO_2	—	Nil	—	15 †
k	NO_2	H	30	79	—	—
l	Cl	Cl	—	65	77	83
m	Me	Cl	—	61	79	86
n	Me	NO_2	—	Nil	—	20 †
o	NO_2	Me	60	88	—	—
p	MeO	NO_2	9	60 †	—	—

† Obtained by fractional crystallisation of the bases (see p. 888).

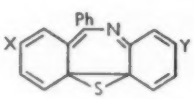
clearly show the scope and value of the method for preparing phenanthridines of this substitution pattern. At the higher temperature variation of the substituent X is seen to be less significant than variation of the substituent Y. The latter, as an electron-donating group, promotes the reaction (d, f, h) but as an electron-restraining group retards it (j, n): on the other hand, X can promote the reaction either as a strongly donor group (g) or as an acceptor group (k). However, at the lower temperature substituent X promotes the reaction more effectively when it is an acceptor group (k, o) than when it is a donor group (g, i). In a reaction at this temperature Brodrick, Nicholson, and Short, who used cuprous salts as catalysts, also failed to detect extrusion of sulphur from the parent thiazepine (Ia) and record only meagre yields of phenanthridines from the thiazepines (I; X = Y = Br or CN).



(III)



(IV)



(V)

The experimental results can be interpreted in terms of the two principal pathways, leading to an intermediate (V) and indicated in formulæ (III) and (IV), by which the carbon atoms initially linked through sulphur become directly linked. Each of the pathways will be affected in a readily accountable manner by the nature of the substituents X and Y, and subsidiary pathways could conceivably be opened by conjugation between these substituents, but the main course is clearly that represented in (III). This predominates at the lower temperature and is perhaps supplemented by course (IV) at the higher temperature. For the subsequent extrusion of sulphur from the intermediate (V) there is analogy in the pyrolysis of arylated ethylene sulphides, a reaction which yields

the corresponding ethylene and is facilitated by the presence of copper:[4] moreover, episulphides are the postulated intermediates in a number of allied reactions[5] which also lead to extrusion of sulphur.

It is noteworthy that in nitrobenzene–phosphoryl chloride the thiazepine (I; X = H, Y = OMe), during the final stage of its preparation (method A), yielded a considerable quantity of 2-methoxy-9-phenylphenanthridine (II; X = H, Y = OMe). On the other hand, attempts to effect extrusion from thiazepines in phosphoric or hydrochloric acid, or from the hydroxythiazepine (Ih) in boiling 2N-sodium hydroxide were unsuccessful.

Experimental

2-Nitrodiaryl Sulphides.—The 2-nitrodiaryl sulphides described in Table 3 were prepared by dropwise addition of 30% aqueous sodium hydroxide (1·1 mol.) to a solution of the appropriate thiophenol (1·1 mol.) and *o*-chloronitrobenzene (1 mol.) in ethanol (500 c.c.), the whole being heated thereafter for 30 min. under reflux and the product crystallised from methanol or ethanol.

TABLE 3. 4- *and/or* 4′-*Substituted 2-nitrodiphenyl sulphides.*

Cross ref.	Subst. 4′	Subst. 4	M. p.	Formula	Found (%) C	Found (%) H	Found (%) N	Required (%) C	Required (%) H	Required (%) N
a	H	H	79° [6]	$C_{12}H_9O_2NS$	—	—	—	—	—	—
b	H	Cl	84 [7]	$C_{12}H_8O_2NSCl$	—	—	—	—	—	—
c	Cl	H	97	,,	54·1	3·2	5·7	54·2	3·0	5·3
d	H	Me	72	$C_{13}H_{11}O_2NS$	63·7	4·3	5·8	63·7	4·5	5·7
e	Me	H	89 [8]	,,	—	—	—	—	—	—
f	H	MeO	Oil *	$C_{13}H_{11}O_3NS$	—	—	—	—	—	—
g	MeO	H	94	,,	59·5	3·9	5·6	59·8	4·2	5·3
l	Cl	Cl	158 [7]	$C_{12}H_7O_2NSCl_2$	—	—	—	—	—	—
m	Me	Cl	121 [9]	$C_{13}H_{10}O_2NSCl$	—	—	—	—	—	—

* The oil was used as such and was characterised by oxidation with hydrogen peroxide in acetic acid to the corresponding *sulphone*, m. p. 105° (Found: C, 53·3; H, 3·8; N, 4·8. $C_{13}H_{11}O_4NS$ requires C, 53·2; H, 3·9; N, 4·8%).

2-Benzamidodiaryl Sulphides.—2-Nitrodiaryl sulphides were reduced [6] to the amines which were isolated as crude hydrochlorides and these were treated with benzoyl chloride at room temperature for 2—3 hr. in dry pyridine. After addition of dilute sulphuric acid and recovery from alkali-washed and dried ethereal extracts, all except the last three benzamido-compounds described in Table 4 were thus obtained. The last three compounds were prepared by the

TABLE 4. 4- *and/or* 4′-*Substituted 2-benzamidodiphenyl sulphides.*

Cross-ref.	Subst. 4′	Subst. 4	M. p.	Formula	Found (%) C	Found (%) H	Found (%) N	Required (%) C	Required (%) H	Required (%) N
a	H	H	67° [1]	$C_{19}H_{15}ONS$	—	—	—	—	—	—
b	H	Cl	81	$C_{19}H_{14}ONSCl$	67·1	4·5	4·3	67·2	4·1	4·1
c	Cl	H	102	,,	67·1	4·7	4·2	,,	,,	,,
d	H	Me	91	$C_{20}H_{17}ONS$	74·9	5·5	4·5	75·2	5·4	4·4
e	Me	H	94	,,	75·1	5·1	4·2	,,	,,	,,
f	H	MeO	61	$C_{20}H_{17}O_2NS$	71·9	5·3	4·2	71·6	5·1	4·2
g	MeO	H	78	,,	71·3	4·9	4·1	,,	,,	,,
l	Cl	Cl	110	$C_{19}H_{13}ONSCl_2$	61·2	3·7	4·0	61·0	3·5	3·7
m	Me	Cl	85	$C_{20}H_{16}ONSCl$	67·5	4·5	4·0	67·9	4·5	4·0
j	H	NO_2	115	$C_{19}H_{14}O_3N_2S$	65·2	4·0	8·3	65·1	4·0	8·0
n	Me	NO_2	125	$C_{20}H_{16}O_3N_2S$	65·6	4·3	7·9	65·9	4·4	7·7
o	MeO	NO_2	142	$C_{20}H_{16}O_4N_2S$	63·2	4·1	7·6	63·1	4·2	7·4

procedure for 2-nitrodiaryl sulphides but by using 2-chloro-5-nitrobenzanilide (suspension) in place of the chloronitrobenzene.

[4] Staudinger and Siegwart, *Helv. Chim. Acta*, 1920, **3**, 833. Schönberg, *Ber.*, 1925, **58**, 1793; Schönberg and Vargha, *Annalen*, 1930, **483**, 176.

[5] Parham and Traynelis, *J. Amer. Chem. Soc.*, 1954, **76**, 4960; 1955, **77**, 68; Knott, *J.*, 1955, 916 *et seq.* Moore and Porter, *J.*, 1958, 2062; Schönberg, *J. Org. Chem.*, 1958, **23**, 104; cf. Huisgen and Appl, *Chem. Ber.*, 1958, **91**, 12.

[6] Roberts and Turner, *J.*, 1926, 1208.

[7] Loudon and Shulman, *J.*, 1938, 1618.

[8] Gilman and Broadbent, *J. Amer. Chem. Soc.*, 1947, **69**, 2053.

[9] Loudon and Robson, *J.*, 1937, 242.

11-*Phenyldibenzo*[b,f]-1 : 4-*thiazepines.*—*Methods* A *and* B, *Table* 1. The 2-benzamidodiaryl sulphide (1 mol.), phosphoryl chloride (4 mol.), and pure nitrobenzene (13 mol.) were heated under reflux for 4 hr. After removal of volatile materials at 0·1 mm. and trituration of the residue with dilute sodium hydroxide the thiazepine was recovered in benzene. By-products were obtained in two cases: (i) The usual trituration of the crude product from 2-benzamido-4-methoxydiphenyl sulphide gave a considerable quantity of a yellow solid which was insoluble in benzene. This solid, after being heated for 30 min. with dilute aqueous sodium hydroxide, yielded 2-methoxy-9-phenylphenanthridine (Table 5) which was recovered in hot benzene: alternatively a hot solution of the original solid in dilute sulphuric acid gave as yellow needles, m. p. 283° (decomp.), the *sulphate* of the same base (Found: C, 62·5; H, 4·25; N, 3·8. $C_{20}H_{15}ON,HSO_4$ requires C, 62·7; H, 4·5; N, 3·65%). (ii) The benzene extract of the crude product from 2-benzamido-4′-methoxy-4-nitrodiphenyl sulphide afforded a small first crop of 5-nitro-2-phenylbenzothiazole, m. p. 138° (from ethanol) (Found: C, 61·1; H, 2·9; N, 10·6. Calc. for $C_{12}H_8O_2N_2S$: C, 61·0; H, 3·15; N, 10·9%). This compound is apparently formed by scission of the diaryl sulphide and cyclisation of the resultant 2-benzamido-4-nitrothiophenol (or its equivalent): the mechanism was not examined.

Method C, *Table* 1. To a solution of 4 : 4′-dimethyl-2 : 2′-dinitrodiphenyl disulphide in glacial acetic acid at 100° successive additions of concentrated hydrochloric acid and zinc dust were made until the solution was colourless. The hot filtered solution was then added to twice its volume of water containing sodium acetate equivalent to the mineral acid used. The resultant zinc salt was dried and dissolved in concentrated hydrochloric acid from which 2-*amino*-4-*methylthiophenol hydrochloride* crystallised; it had m. p. 189° (decomp.) (Found: C, 47·6; H, 5·5; N, 7·8. C_7H_9NS,HCl requires C, 47·9; H, 5·7; N, 8·0%). It was condensed with 2-chloro-5-nitrobenzophenone as described for the lower homologue.

2- and 8-Hydroxythiazepine (Ii, Ih, Table 1) were obtained by demethylating 2- and 8-methoxythiazepine with hydrobromic acid in acetic acid (3 hr. under reflux).

9-*Phenylphenanthridines.*—A small pear-shaped flask, containing the thiazepine (0·001 mole), copper bronze (0·4 g.), and diethyl phthalate (3 c.c.) in an atmosphere of nitrogen, was plunged into a metal-bath regulated at 315°. Thereupon the bath temperature fell to 300° and then slowly rose again. After the stated time (Table 2) the flask was removed, its contents were cooled, transferred, and boiled with benzene, and the resultant suspension was filtered through a pad of charcoal. For the phenanthridines (II, a–h, l, and m; Tables 2 and 5) the filtrate was

TABLE 5. 9-*Phenylphenanthridines* (II).

	Subst.				Found (%)			Required (%)			Picrate
(II)	X	Y	M. p.	Formula	C	H	N	C	H	N	M. p.
a	H	H	105° [1]	$C_{19}H_{13}N$	—	—	—	—	—	—	251°
b	H	Cl	134	$C_{19}H_{12}NCl$	79·1	4·3	4·7	78·7	4·1	4·8	245
c	Cl	H	120 [11]	,,	—	—	—	—	—	—	260
d	H	Me	119 [12]	$C_{20}H_{15}N$	—	—	—	89·2	5·6	—	245
e	Me	H	90	,,	89·3	5·4	—	,,	—	—	280
f	H	MeO	116	$C_{20}H_{15}ON$	84·1	5·5	5·1	84·2	5·3	4·9	260 *
g	MeO	H	Oil [13]	,,	—	—	—	—	—	—	270
h	H	HO	290	$C_{19}H_{13}ON$	83·9	5·0	5·0	84·1	4·8	5·2	295
i	HO	H	266	,,	83·8	4·7	5·2	,,	,,	,,	245 †
j	H	NO_2	223	$C_{19}H_{12}O_2N_2$	76·3	3·8	9·3	76·0	4·0	9·3	215
k	NO_2	H	236 [3]	,,	—	—	—	—	—	—	247
l	Cl	Cl	196	$C_{19}H_{11}NCl_2$	70·4	3·9	4·4	70·4	3·4	4·3	214
m	Me	Cl	179	$C_{20}H_{14}NCl$	79·1	4·6	4·6	79·3	4·6	4·6	232
n	Me	NO_2	228	$C_{20}H_{14}O_2N_2$	76·3	4·9	8·9	76·4	4·5	8·9	209
o	NO_2	Me	229	,,	76·3	4·7	9·0	,,	,,	,,	213
p	MeO	NO_2	213	$C_{20}H_{14}O_3N_2$	72·7	4·0	8·6	72·7	4·3	8·5	231

* Found: C, 60·5; H, 3·7. $C_{26}H_{19}O_8N_4$ requires C, 60·7; H, 3·5%.
† Found: C, 59·4; H, 3·1. $C_{25}H_{16}O_8N_4$ requires C, 60·0; H, 3·2%.

concentrated to 25 c.c. and treated with a saturated solution (4 c.c.) of picric acid in benzene, the picrate being collected after 30 min. and weighed. In the other cases (II, i, j, k, n, o, p) picrate precipitation was incomplete even after 12 hr. and successive crops were obtained by

[10] Fries, Koch, and Stuckenbrock, *Annalen*, 1929, **468**, 201.
[11] Mamalis and Petrow, *J.*, 1950, 703.
[12] Ritchie, *Proc. Roy. Soc. N.S. Wales*, 1945, **78**, 134.
[13] Copp and Walls, *J.*, 1950, 311.

further concentration: alternatively the solvents were removed (120°/0·1 mm.) from the original benzene filtrate, and the resultant bases were fractionally crystallised from ethanol. Phenanthridines (Table 5), liberated from picrates by treatment with alkali, were recovered in benzene.

Reactions in quinoline were similarly conducted (bath-temp. 255°), solvents being removed *in vacuo* from the benzene–quinoline filtrate and the residue, dissolved in benzene, being washed with 1·5N-acetic acid. Phenanthridines—except for the cases (k, o, p, Table 2) where the free bases were fractionally crystallised—were precipitated as picrates, and thereafter unchanged thiazepines were recovered from the alkali-washed benzene mother-liquor.

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THE UNIVERSITY, GLASGOW, W.2. [*Received, November 3rd*, 1958.]

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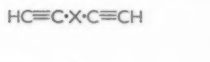
182. *Macrocyclic Acetylenic Compounds. Part I.* cyclo*Tetradeca*-1 : 3-*diyne and Related Compounds.*

By G. EGLINTON and A. R. GALBRAITH.

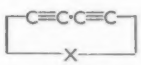
A high-dilution modification of the conventional Glaser procedure for the oxidative coupling of ethynyl compounds has been used in the synthesis of new macrocyclic systems containing the αγ-diyne unit, notably the hydrocarbons *cyclo*tetradeca-1 : 3-diyne (IIa; $n = 10$) and *cyclo*octacosa-1 : 3 : 15 : 17-tetrayne (IIIa; $n = 10$), and the macrolides (IIb and IIIb).

IN a preliminary announcement,[1a] we reported the synthesis of a number of macrocyclic compounds containing the αγ-diyne unit. The present paper gives a full account of this work and of more recent results. Sondheimer and his collaborators[1b] have described independent studies which have also led to cyclic αγ-diynes.

Medium-sized carbocyclic compounds containing an acetylenic linkage are well known,[2] *cyclo*octyne being the smallest so far obtained. However, at the commencement of these researches, no cyclic αγ-diyne had been described, though such compounds would be of particular interest for the study of the correlations of their physical and chemical properties with the degree of ring strain. Further, the presence of other groups within the ring would introduce the possibility of transannular phenomena.



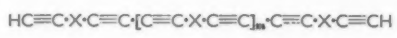
(I)



(II)

(III)

a, X = $[CH_2]_n$. b, X = $[CH_2]_2{\cdot}O{\cdot}CO{\cdot}[CH_2]_3{\cdot}CO{\cdot}O{\cdot}[CH_2]_2$. c, X = $[CH_2]_n{\cdot}O{\cdot}CO{\cdot}C_6H_4{\cdot}CO{\cdot}O{\cdot}[CH_2]_n$ (p)



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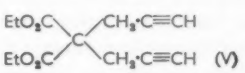

(V)

Although ethynyl compounds and their derivatives have been coupled in other ways[3,4] the obvious approach to systems of type (II) is clearly the oxidative coupling of αω-diethynyl compounds (I); this reaction has been extensively employed[3] in the synthesis of

[1] (*a*) Eglinton and Galbraith, *Chem. and Ind.*, 1956, 737; (*b*) Sondheimer, Amiel, and Wolovsky, *J. Amer. Chem. Soc.*, 1957, **79**, 4247 and preceding papers.

[2] Blomquist *et al.*, *J. Amer. Chem. Soc.*, 1951, **73**, 5510; 1952, **74**, 3636, 3643; 1953, **75**, 2153; Prelog *et al.*, *Helv. Chim. Acta*, 1952, **35**, 1598; 1953, **36**, 471; 1955, **38**, 1776, 1786; Cram *et al.*, *J. Amer. Chem. Soc.*, 1955, **77**, 4090; 1956, **78**, 2518; Epstein and Marszak, *Compt. rend.*, 1956, **243**, 283.

[3] Raphael, "Acetylenic Compounds in Organic Synthesis," Butterworths, London, 1955.

[4] Chodkiewicz, *Ann. Chim.* (*France*), 1957, **2**, 819; Cadiot and Chodkiewicz, *Compt. rend.*, 1957, **245**, 1634.

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acyclic αγ-diynes, $2R{\cdot}C{\equiv}CH \longrightarrow R{\cdot}C{\equiv}C{\cdot}C{\equiv}C{\cdot}R$, normally by agitating a suspension of the ethynyl compound in a mixture of cuprous chloride, ammonium chloride, and water in air or oxygen: water-soluble ethynyl compounds, *e.g.*, $HC{\equiv}C{\cdot}CMe_2{\cdot}OH$, couple rapidly and almost quantitatively, whereas water-insoluble compounds, *e.g.*, alk-1-ynes, frequently do so only with difficulty.[5]

The mechanism of this reaction has received serious attention only recently. In 1955, Baxendale and Westcott [6] showed that cupric ion is the oxidising agent; with stoicheiometric quantities of cupric ion in an aqueous medium buffered to pH 6 to avoid inhibition of the reaction by developing acidity, the αγ-diyne was rapidly formed in 50% yield, the remainder of the ethynyl compound being converted into the insoluble cuprous derivative:

$$4R{\cdot}C{\equiv}CH + 2Cu^{+2} \longrightarrow R{\cdot}C{\equiv}C{\cdot}C{\equiv}C{\cdot}R + 2R{\cdot}C{\equiv}C{\cdot}Cu + 4H^{+}$$

The latter is then available for slow oxidation to the αγ-diyne by excess of cupric ion, oxygen, or other oxidising agent, giving the overall reaction:

$$2R{\cdot}C{\equiv}CH + 2Cu^{+2} \longrightarrow R{\cdot}C{\equiv}C{\cdot}C{\equiv}C{\cdot}R + 2H^{+} + 2Cu^{+}$$

For successful cyclisation of αω-diynes the coupling should be in homogeneous solution under high-dilution conditions, in order to avoid the formation of much polymer (IV) and of insoluble cuprous salts. The formation of cyclic products might be further assisted by the rigid nature of the four-atom system C–C≡C–H, which would reduce the number of possible molecular conformations.[7]

A solvent capable of retaining in solution the ethynyl compound, some form of cupric ion, and the intermediate cuprous derivative was found with anhydrous cupric acetate in methanol–pyridine. The pyridine–cupric ion complex appeared to be solvated by the methanol, rendering possible extensive dilution with the ether used as the entraining agent in the high-dilution apparatus. The pyridine also served to remove the acetic acid liberated in the coupling reaction. These experiments were conducted with the readily available 2-methylbut-3-yn-2-ol and phenylacetylene. Virtually quantitative yields of the highly crystalline αγ-diynes were obtained by using catalytic quantities of the cupric ion in solution and continuously oxidising the soluble cuprous derivative in a stream of oxygen. However, for general preparative purposes, it was more convenient to use excess of the reagent. Only occasionally was the formation of a small amount of reddish-brown precipitate (presumably cuprous derivative) observed, and the reaction mixtures were otherwise homogeneous. Solutions of ferric and cobaltic salts and of strongly complexed cupric ion (salicylate and ethylenediamine complexes) were ineffective.

The reagent was now employed in the cyclisation of an αω-diyne, the intention being either to add the substance at a rate such that it underwent immediate reaction or, less satisfactorily, to continue reaction until ethynyl groupings would be no longer detectable. The sebacic diester (Ib) proved to be readily accessible, stable and highly crystalline and, from an examination of models, the derived cyclic monomer (IIb) appeared to be strainless. Slow entrainment of the ester in refluxing solvent evidently resulted in satisfactory high-dilution conditions during the oxidative coupling, as the product appeared to consist largely of the cyclic monomer (IIb), m. p. 54·5°, which was readily isolated in 63% yield.* In another experiment, the cyclic dimer (IIIb), m. p. 109—110°, was also obtained, in about 2% yield. The structures were inferred from the method of preparation, and from analyses, light-absorption characteristics, and Rast molecular-weight determinations. Although suitable reference substances were not available to allow of proof by hydrogenation, it is clear that these colourless, highly crystalline substances provided the first

* The terms "monomer," "dimer," etc., are here used to denote the cyclic compounds $\ulcorner[C{\equiv}C{\cdot}X{\cdot}C{\equiv}C]_n\urcorner$ derived from the true acyclic monomer $HC{\equiv}C{\cdot}X{\cdot}C{\equiv}CH$.

[5] Bowden, Heilbron, Jones, and Sargent, *J.*, 1947, 1579; Salkind and Fundyler, *Ber.*, 1936, **69**, 128.
[6] Baxendale and Westcott, personal communication.
[7] Baker, McOmie, and Ollis, *J.*, 1951, 200.

examples of macrocycles containing the αγ-diyne unit. The conventional cuprous chloride–ammonium chloride procedure for coupling gave only starting material and polymer.

The synthesis of a *cyclo*alka-1 : 3-diyne (IIa), the ring size of which would allow of proof by hydrogenation to a known *cyclo*alkane, was next attempted. From consideration of " Catalin " models, *cyclo*tetradeca-1 : 3-diyne (IIa; $n = 10$) was chosen in the belief that the chain of ten methylene units would be long enough to allow the ring to be reasonably free from strain. Tetradeca-1 : 13-diyne (Ia; $n = 10$), m. p. 33—34°, readily obtained from decamethylene dibromide and sodium acetylide in liquid ammonia at 20°, coupled much more slowly than the ester (Ib): it was adequate and convenient to put the substance aside, in a large volume of the reagent for several days. The crude product (*ca.* 50% yield) appeared to be largely cyclic (absence of ethynyl absorption at 3300 cm.$^{-1}$) and was separated by chromatography into monomer (IIa; $n = 10$), m. p. 18°, and the dimer (IIIa; $n = 10$), m. p. 101—102°. These structures followed unambiguously from the analytical data and light-absorption characteristics and from the identity of the fully hydrogenated hydrocarbons with *cyclo*tetradecane and *cyclo*octacosane respectively. *cyclo*Tetradeca-1 : 3-diyne was generally the chief product, though the yield (17—40%) varied according to the degree of dilution. Liquid at room temperature, the hydrocarbon rapidly reddened in air with the simultaneous appearance of carbonyl absorption at 1735 cm.$^{-1}$. This instability is probably associated with ring strain as the corresponding dimer was much more stable.

Three esters (Ic; $n = 1$, 2, and 4) were next prepared and intramolecular couplings attempted. It was hoped that a suitable cyclic monomer might exhibit some abnormalities [1b] resulting from transannular interaction, particularly between the benzene ring and the αγ-diyne unit. The ester linkages proved unexpectedly labile under cyclisation conditions, as even in pyridine alone the esters (Ic; $n = 1$ or $= 2$) gave complicated tarry mixtures. The dihexynyl ester (Ic; $n = 4$), under high-dilution conditions in pyridine–methanol, was largely converted into dimethyl terephthalate and dodeca-5 : 7-diyne-1 : 12-diol, presumably as a result of pyridine-catalysed ester interchange. When the methanol was omitted, a new substance (30% yield), m. p. 210—211°, was isolated which, from the analytical, molecular weight and light absorption data, was clearly the dimer (IIIc; $n = 4$). A few milligrams of another substance, m. p. 145—148°, believed to be the monomer (IIc; $n = 4$), were also isolated, but no support for this supposition is available.

It is surprising that identifiable compounds could not be isolated from the reaction mixtures derived from the esters (Ic; $n = 1$ and 2) and that the dimer was obtained almost to the exclusion of the monomer in the case of (Ic; $n = 4$). Presumably internal strains resulting from unfavourable dipolar interactions render difficult the formation of the smaller rings and may also occasion their decomposition during the removal of the rather large bulk of solvent necessitated by the high-dilution procedure.

Several attempts to isolate identifiable substances from the coupling of the ester (V) have been frustrated as the resulting red oil, though substantially " coupled " (absence of free ethynyl groups), decomposed rapidly at room temperature and no evidence as to its constitution could be obtained.

The light absorption of the αγ-diyne unit in a cyclic compound (cf. Table 1) might be expected to indicate any molecular abnormalities, for example, ring strain and transannular interaction. However, αγ-diynes are reported [8] as having only weak ultraviolet and infrared [12] absorption ($\lambda_{max.}$ approx. 228, 238, and 254 mμ, ε 300—400, 300—400, and 180—240; $\nu_{max.}$ at 2230 and 2140 cm.$^{-1}$).

Measurements in the 200—230 mμ region are subject to certain instrumental difficulties and are likely to be somewhat inaccurate.[9] Further, the weak diyne absorption is easily interfered with by absorption due to strongly absorbing impurities,

[8] Armitage, Cook, Entwistle, Jones, and Whiting, *J.*, 1952, 1998.
[9] Eglinton, Jones, and Whiting, *J.*, 1952, 2873.

readily formed by oxidation or hydration of the αγ-diyne; enynes ($\lambda_{max.}$ 228 mμ, ε 14,000), now obtainable on a preparative scale by dimerisation of ethynyl compounds under conditions rather similar to those employed in the oxidative coupling,[10] probably contaminate αγ-diynes prepared in this way. Variations in ε values which have been

TABLE 1. *Physical characteristics of macrocyclic αγ-diynes.*

Diyne	M. p.	Yield (%)	$\lambda_{max.}$ (mμ)	ε/unit *	$\lambda_{max.}$ (mμ)	ε/unit *	$\lambda_{max.}$ (mμ)	ε/unit *
(IIa; $n = 10$)...	18°	17—40	230	690	242	600	257	440
(IIIa; $n = 10$)	101—102	10—30	226	490	239	465	254	320
(IIb)	54—55	63	226	686	238	551	254	225
(IIIb)	109—110	2	225	415	240	375	254	190

* Per diyne unit.

encountered in the present work are probably to be attributed to one or more of the above causes. Previously [1a] we quoted ($\lambda_{max.}$ 226 mμ, ε 1357 in hexane) for (IIb), though later material of lower ε resulted. Chromatography and crystallisation of the highly crystalline cyclic di-yne (IIb) failed markedly to change the ε values, which are now in reasonable accord with those for an open-chain αγ-diyne. The original values are explicable if the presence of *ca.* 5% of enyne is assumed. The only compound in the present series likely to be subject to ring strain (IIa; $n = 10$) has absorption maxima shifted about 3 mμ to longer wavelength, though it is doubtful whether this shift has much significance.

In small-ring lactones ring strain raises the carbonyl stretching frequencies (6-, 5-, and 4-membered lactone rings have absorption maxima at 1740, 1765, and 1800 cm.$^{-1}$ respectively [12]), but in larger rings conformational effects and steric interactions may be important and may have the reverse effect. The ester (Ic; $n = 4$) and the large-ring lactone (IIIc; $n = 4$) have virtually the same carbonyl frequency (cf. Table 2), while the values for the compounds (Ib, IIb, and IIIb) differ by only small amounts. It is evident that in (IIb) ring strain if present has had no effect; the " Catalin " model of (IIb) is not strained and several orientations for the ester groupings including the stable *s-trans*-conformation, are possible.

TABLE 2. *Carbonyl stretching frequencies* (*in* CCl_4).

Compound	ν (cm.$^{-1}$)	$\Delta\nu_{\frac{1}{2}}^{A}$ † (cm.$^{-1}$)	ε_A †	Compound	ν (cm.$^{-1}$)	$\Delta\nu_{\frac{1}{2}}^{A}$ † (cm.$^{-1}$)	ε_A †
(Ic; $n = 4$) ...	1726	16	1140	(IIIb)	1743	Not measured	
(IIIc; $n = 4$)	1727	Very sparingly soluble		* Acetone	1719	18	246
(Ib)	1745	18	855	* *cyclo*Pentan-one	1751	24	288
(IIb)	1742	18	980				

* Reference standard for calibration.[11]

† $\Delta\nu_{\frac{1}{2}}^{A}$ apparent half band width; ε_A apparent molecular extinction coefficient = $(1/cl) \log_{10} (T_0/T)_\nu$.

The αγ-diyne C≡C stretching frequencies seem to be relatively insensitive to the nature of substituent groups and are of such low intensity ($\varepsilon < 10$) that they may be masked by overtone and combination bands, particularly in aromatic and oxygenated substances. The cyclic compounds seemed normal (cf. Table 3); for example, the hydrocarbon (IIIa; $n = 10$) has weak bands at 2250 and 2140 cm.$^{-1}$ (in Nujol): Sondheimer and Amiel [13] give 2228 and 2142 cm.$^{-1}$ for dodeca-5 : 7-diyne (in $CHCl_3$).[14]

After our preliminary communication [1a] Sondheimer and his collaborators described a parallel investigation.[1b] Employing αω-diynes of shorter chain length (Ia; $n = 3$, 4, and 5) and the conventional cuprous chloride–ammonium chloride coupling reagent, they

[10] Dr. B. C. L. Weedon, personal communication.
[11] Bellamy and Williams, *J.*, 1957, 4294.
[12] Bellamy, " The Infra-red Spectra of Complex Molecules," Methuen, London, 1958.
[13] Sondheimer and Amiel, *J. Amer. Chem. Soc.*, 1957, **79**, 5817.
[14] Sheppard and Simpson, *Quart. Rev.*, 1952, **6**, 1.

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isolated, not only the corresponding acyclic dimers, trimers, and tetramers (IV), but also, though in small yield, the cyclic dimer (IIIa; $n = 3$). The diynes (Ia; $n = 2$ and 6) failed to give cyclic products. However, our cupric acetate reagent with relatively high concentrations of the diynes (Ia; $n = 2$—5) gave products consisting almost entirely of cyclic polymers ranging from dimers (IIIa; $n = 4$) to hexamers ($n = 5$). The fact that

TABLE 3. ν (C≡C) *of αγ-diynes.*

Compound	In CCl_4 cm.$^{-1}$	In CCl_4 $\Delta\nu_{\frac{1}{2}}^{A}$ cm.$^{-1}$	In CCl_4 ε_A	In Nujol cm.$^{-1}$	In Nujol $\Delta\nu_{\frac{1}{2}}^{A}$ cm.$^{-1}$
Ph·C≡C·C≡C·Ph	2222	35	2·3	Very weak	
	2132	20	3·5	2130	19
Ph·C≡C·C≡C·CMe_2·OH	2235	16	7·4	—	—
	2132	30	0·7	—	—
HO·CMe_2·C≡C·C≡C·CMe_2·OH	Insoluble		—	2251	14
				2124	21
HO·$[CH_2]_4$·C≡C·C≡C·$[CH_2]_4$·OH	Insoluble		—	2171(?)	~50
				2120	~50
AcO·$[CH_2]_4$·C≡C·C≡C·$[CH_2]_4$·OAc	2258, 2204, 2150 Complex		2	Overtone bands causing confusion	
(IIb)	2256	30	1·3	—	—
	2150	33	1·5	—	—
(IIIa; $n = 10$)	—	—	—	2250	~60
				2140	~30
CH_2=CH·CN (liquid) *	2228	11	—	—	—

* Standard for reference (Halverson, Stamm, and Whalen, *J. Chem. Phys.*, 1948, **16**, 808.

the homogeneous reagent favours the formation of cyclic products must have some bearing on the mechanism. Klebanski *et al.*[15] postulated that in aqueous solutions the reaction of ethynyl compounds with cupric ion proceeds as follows:

$$\text{(i)}\ R{\cdot}C{\equiv}CH \underset{}{\overset{\text{Slow}}{\rightleftharpoons}} R{\cdot}C{\equiv}C^- + H^+$$

$$\text{(ii)}\ R{\cdot}C{\equiv}C^- + Cu^{+2} \xrightarrow{\text{Fast}} R{\cdot}C{\equiv}C{\cdot} + Cu^+$$

$$\text{(iii)}\ 2R{\cdot}C{\equiv}C{\cdot} \xrightarrow{\text{Fast}} R{\cdot}C{\equiv}C{\cdot}C{\equiv}C{\cdot}R$$

Stages (i) and (ii) involve complex copper derivatives rather than the simple anion. However, it seems hardly possible that a cyclic cuprous salt could exist during the formation of (IIa; $n = 10$), the cyclisation presumably occurring as a result of the transitory formation of a diradical $\cdot C{\equiv}C{\cdot}[CH_2]_{10}C{\equiv}C{\cdot}$. Klebanski *et al.* showed that the more acidic the ethynyl compound the more rapidly it coupled, *e.g.*, Ph·C≡CH > $Me_2C(OH)$·C≡CH, a fact which we had noted and is in accord with a rate-determining stage (i).

Further work is in progress.[16] The cupric acetate reagent also appears advantageous in the coupling of monoethynyl compounds.[17]

EXPERIMENTAL

M. p.s were taken on the Kofler block. The alumina for chromatography was acid-washed, neutralised, and standardised according to Brockmann's method; grade 5 was used unless otherwise stated. Light petroleum was of b. p. 40—60°. Molecular weights were obtained by the Rast method [*ca.* 7 mg. in camphor (50 mg.)]. Ultraviolet absorption spectra refer to solutions in hexane determined on the Unicam S.P. 500 spectrophotometer, infrared measurements (Perkin-Elmer, Model 13) to mulls in " Nujol " unless stated to the contrary. Precise frequency and ε determinations in solution were made with the Unicam S.P. 100 spectrophotometer (sodium chloride prism). Sublimations were performed at 10^{-4} mm.

[15] Klebanski, Grachev, and Kustretsova, *Zhur. obshchei Khim.*, 1957, **27**, 2977.
[16] Eglinton and Galbraith, *Proc. Chem. Soc.*, 1957, 350.
[17] Bohlman *et al.*, *Ber.*, 1957, **90**, 130, 1661.

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Oxidative Coupling of 2-Methylbut-3-yn-2-ol by Cupric Ion.—(i) *In water at* pH 5·6 (*conditions suggested by* Dr. J. H. Baxendale). The alcohol (5 g.) was added to a stirred solution of cupric sulphate pentahydrate (12·5 g.), sodium acetate trihydrate (34 g.), acetic acid (1·5 g.), and cuprous chloride (0·5 g.) in water (500 c.c.). The mixture was kept at 70° for 30 min., the precipitated cuprous derivative (3·3 g., 36%) was removed, and the green filtrate extracted with ether. After removal of the solvent, crystalline 2 : 7-dimethylocta-3 : 5-diyne-2 : 7-diol (2·9 g., 58%) remained. Recrystallisation from ether–light petroleum gave the pure diol,[18] m. p. 130—131°.

(ii) *In organic solvents.* (*a*) 2-Methylbut-3-yn-2-ol (400 mg.) was added to a solution of anhydrous cupric acetate [19] (2 g.) in pyridine–methanol–ether (1 : 1 : 4; 200 c.c.) and heated under reflux for 20 min. After removal of the bulk of the solvent under reduced pressure, the residue was acidified and extracted with ether, and the extract evaporated to give the diol, m. p. 128—130° (350 mg., 88%).

(*b*) A solution of the alcohol (805 mg.) and cupric acetate (10 mg.) in pyridine–methanol–ether (1 : 1 : 3; 50 c.c.) was heated under reflux for 7 hr. in a stream of oxygen. The diol (645 mg., 80%) was isolated in the usual way.

(*c*) The cupric salts of inorganic acids had low solubilities in pyridine. Cupric butyrate,[20] stearate, naphthenate, and benzoate [20] were soluble in varying degrees in the solvent and in benzene. However, removal of the corresponding acids from the reaction mixtures presented a complication. Cupric salicylate and the ethylenediamine salt proved ineffective.

Oxidative Coupling of the Cuprous Derivative of Phenylacetylene.—The cuprous derivative (1 g.) of phenylacetylene was added in pyridine (60 c.c.) to cupric acetate (2 g.) in hot pyridine (60 c.c.). The resulting green solution was heated for 20 min. at 90°, then cooled, and the product isolated in the usual way. Diphenyldiacetylene (350 mg., 70%) separated in prisms, m. p. 84—86° (Glaser [21] gives 88°) (from aqueous ethanol).

Dibut-3-yn-1-yl Sebacate (Ib).—Pyridine (10·5 g.) was added dropwise to a stirred solution of sebacoyl chloride (13·3 g., freshly prepared; b. p. 128—134°/0·3 mm.) in dry ether (150 c.c.) containing but-3-yn-1-ol (8 g.). After removal of the precipitated pyridine hydrochloride, the neutral fraction was isolated as an ethereal solution and passed down a column of alumina. The *ester* (11 g., 61%) crystallised from ether in plates, m. p. 65—65·5° (Found: C, 70·5; H, 8·4. $C_{18}H_{26}O_4$ requires C, 70·6; H, 8·5%), $\nu_{max.}$ (in Nujol) 3260 (≡CH), 2100 (–C≡CH), and 1740 cm.$^{-1}$ (ester).

High-dilution Oxidative Coupling of Dibut-3-yn-1-yl Sebacate (Ib) (with W. McCrae).—A solution of the sebacate (1 g.) in ether–pyridine (1 : 6; 140 c.c.) was added during 2½ hr. to a refluxing solution of anhydrous cupric acetate (3·4 g.) in ether–pyridine (1 : 6; 700 c.c.), the drops of ester solution being continuously entrained by the refluxing solvent in a modified continuous-extraction apparatus. After a further hour the resulting green solution was cooled and slowly added, with stirring, to 0·05N-hydrochloric acid (5 l.) at 0°, and the neutral fraction isolated with ether, and its solution in benzene passed through alumina (grade III; 30 g.), the final elution being with ether–benzene. The solvent was removed and the residual solid recrystallised from light petroleum, giving *octa-3 : 5-diynylene sebacate* (IIb) (630 mg., 63%) as tablets, m. p. 55—56° (Found: C, 71·2; H, 7·9%; *M*, 334. $C_{18}H_{24}O_4$ requires C, 71·1; H, 7·9%; *M*, 304), $\nu_{max.}$ 2120 (C≡C) and 1720 cm.$^{-1}$ (ester), and $\lambda_{max.}$ (the characteristic three diyne maxima) 226, 238, and 254 mμ (ε 686, 551, and 225 respectively). A solution of the compound in ethyl acetate absorbed 95% of the calculated volume of hydrogen during 10 min. over Adams platinic oxide, whereupon absorption ceased.

Under conditions of lower dilution a cyclic dimer *bisocta-3 : 5-diynylene bis-sebacate* (IIIb) was also isolated (*ca.* 9%). After chromatography it crystallised from light petroleum as prisms, m. p. 109—110° (Found: C, 71·0; H, 8·0%; *M*, 653. $C_{36}H_{48}O_8$ requires *M*, 608), $\nu_{max.}$ 2140 (C≡C) and 1720, 1740 (doublet; ester) cm.$^{-1}$, $\lambda_{max.}$ 225, 240, and 254 mμ (ε 830, 750, and 380 respectively).

An attempt to effect coupling in aqueous dioxan by cuprous chloride–ammonium chloride in oxygen at room temperature led to the recovery of most of the ester. The remainder of the product was ether-insoluble and presumably polymeric. The same reaction at 70° in a

[18] Straus, Kollek, and Hauptmann, *Ber.*, 1930, **63**, 1886.
[19] Spath, *Sitzungsber. Akad. Wiss. Wien*, 1911, **120**, 1117.
[20] Crawford, *Nature*, 1950, **165**, 728.
[21] Glaser, *Ber.*, 1869, **2**, 422; *Annalen*, 1870, **154**, 159.

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predominantly aqueous medium gave a crystalline, probably short-chain polymer (IV), m. p. *ca.* 100° (*ca.* 25%), $\nu_{max.}$ 3300 cm.$^{-1}$ (ethynyl group), which was not examined further.

Tetradeca-1 : 13-diyne (Ia; $n = 10$).—1 : 10-Dibromodecane (25 g.) in ether (40 c.c.) was kept with sodium acetylide (from sodium, 6 g.) in liquid ammonia (500 c.c.) in an autoclave for 24 hr. After the ammonia had been allowed to evaporate and ammonium chloride added, the neutral fraction was isolated with ether. The *hydrocarbon* (9 g., 57%) solidified and a sample was obtained as plates, m. p. 33—34°, after low-temperature crystallisation from light petroleum followed by sublimation (Found: C, 88·7; H, 11·3. $C_{14}H_{22}$ requires C, 88·4; H, 11·6%), $\nu_{max.}$ 3274 and 2100 (C≡CH) cm.$^{-1}$. Canonica *et al.*[22] had previously obtained this compound, *via* the corresponding diene, as a liquid.

Oxidative Coupling of Tetradeca-1 : 13-diyne (Ia; $n = 10$).—Tetradeca-1 : 13-diyne (1 g.) was heated with cupric acetate (4 g.) in pyridine (100 c.c.), methanol (600 c.c.), and ether (800 c.c.) for 72 hr., with continuous passage of a slow stream of oxygen. A small sample had still the same ethynyl content. The solvent was removed and the residue heated in fresh pyridine (500 c.c.) for 72 hr. (ethynyl content now small). Most of the pyridine was then removed from the brown solution under reduced pressure and the residue carefully acidified with hydrochloric acid and extracted with ether. The neutral red oil was chromatographed in light petroleum on alumina, giving in the early fractions oily *cyclotetradeca-1 : 3-diyne* (IIa; $n = 10$) (170 mg., 17%), which after evaporative distillation formed prisms, m. p. 18° (Found: C, 89·1; H, 10·4. $C_{14}H_{20}$ requires C, 89·4; H, 10·6%), $\nu_{max.}$ 2215 and 2132 cm.$^{-1}$ ($\alpha\gamma$-diyne), $\lambda_{max.}$ 230, 242, and 257 mμ (ε 690, 600, and 440 respectively). Later fractions gave *cyclooctacosa-1 : 3 : 15 : 17-tetrayne* (IIIa; $n = 10$) (300 mg., 30%), needles, m. p. 101—102° (from methanol–ether) (Found: C, 89·1; H, 10·5%; *M*, 395. $C_{28}H_{40}$ requires *M*, 376), $\nu_{max.}$ 2252 and 2140 cm.$^{-1}$ ($\alpha\gamma$-diyne), $\lambda_{max.}$ 226, 239, and 254 mμ (ε 980, 930, and 640 respectively).

*cyclo*Tetradeca-1 : 3-diyne (128 mg.) in ethyl acetate (PtO_2) absorbed 90% of the calculated volume of hydrogen. On chromatography of the crude product in light petroleum on alumina, *cyclo*tetradecane (30 mg., 23%), subliming as plates, m. p. 54—55°, undepressed on admixture with a genuine sample (kindly provided by Professor V. Prelog), was obtained. The residue was a petroleum-insoluble acidic oil. *cyclo*Octacosa-1 : 3 : 15 : 17-tetrayne (75 mg.) similarly gave *cyclo*octacosane (20 mg., 25%), which sublimed as plates, m. p. 47—48° (Ruzicka *et al.*[23] give 48°).

Diprop-2-yn-1-yl Terephthalate (Ic; $n = 1$).—Terephthaloyl chloride (8 g.) was added portionwise to an ice-cold solution of prop-2-yn-1-ol (5·5 g.) in 10% aqueous sodium hydroxide (180 c.c.). After 30 min. the precipitate was collected and dissolved in ether, and the neutral fraction isolated. The *ester* (6 g., 63%), after further purification over alumina, separated from methanol in needles, m. p. 107—108° raised on sublimation to 108—109° (Found: C, 69·6; H, 4·1. $C_{14}H_{10}O_4$ requires C, 69·4; H, 4·1%), $\lambda_{max.}$ 242, 285, and 295 mμ (ε 21,000, 1800, and 1500 respectively), $\nu_{max.}$ 3230, 2105, and 1710 cm.$^{-1}$.

Dibut-3-yn-1-yl Terephthalate (Ic; $n = 2$).—Terephthaloyl chloride (3 g.) and but-3-yn-1-ol (2·4 g.) in aqueous sodium hydroxide (60 c.c.) similarly gave the *ester* (2 g., 48%) as needles, m. p. 114—115° (from methanol) (Found: C, 71·3; H, 5·2. $C_{16}H_{14}O_4$ requires C, 71·1; H, 5·2%), $\lambda_{max.}$ 242, 285, and 295 (ε 21,000, 1800, and 1500 respectively), $\nu_{max.}$ 3240, 2100, and 1710 cm.$^{-1}$.

Dihex-5-yn-1-yl Terephthalate (Ic; $n = 4$).—Terephthaloyl chloride (5 g.) and hex-5-yn-1-ol[9] (5 g.) in aqueous sodium hydroxide (100 c.c.) gave, as above, the *ester* (6 g., 80%), needles, m. p. 87—88° (from methanol) (Found: C, 73·7; H, 6·4. $C_{20}H_{22}O_4$ requires C, 73·6; H, 6·7%), $\lambda_{max.}$ 242, 285, and 295 mμ (ε 21,000, 1800, and 1500 respectively), $\nu_{max.}$ 3240, 2210, 2100, and 1720 cm.$^{-1}$.

Oxidative Coupling of Diprop-2-yn-1-yl Terephthalate (Ic; $n = 1$).—A solution of the ester (2 g.) in pyridine–ether (1 : 2; 100 c.c.) was added (3 hr.) under high-dilution, reflux conditions to a solution of cupric acetate (5 g.) in pyridine–ether (7 : 1; 600 c.c.), and refluxing was continued for a further 20 hr. The solution, now free from ethynyl compounds (absence of absorption at 3300 cm.$^{-1}$), was acidified at 0° and extracted with ether. Much black, polymeric, ether-insoluble material remained, while the neutral fraction deposited further quantities of brown polymer. The residual oil was chromatographed (benzene, then chloroform) over alumina and gave only a few mg. of an intractable brown gum.

[22] Canonica, Martinolli, and Bachetti, *Atti Accad. naz. Lincei, Rend. Classe Sci. fis. mat. nat.*, 1952, **13**, 61; *Chem. Abs.*, 1953, **47**, 11131.
[23] Ruzicka, Stoll, Huyser, and Boekenoogen, *Helv. Chim. Acta*, 1930, **13**, 1152.

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In another experiment, when refluxing was for a further 1·5 hr., colourless needles (25 mg.), m. p. 135—137° (Found: C, 63·9; H, 6·2%), were isolated. Light-absorption data were in agreement with formulation of this substance as a non-acetylenic terephthalate derivative.

Oxidative Coupling of Dibut-3-yn-1-yl Terephthalate (Ic; $n = 2$).—In an experiment similar to that above, dibut-3-yn-1-yl terephthalate (2 g.) was added to a solution of cupric acetate (4 g.) in pyridine (600 c.c.). Some precipitation of yellow cuprous salt was noticed during the reaction. The neutral fraction again yielded a small quantity of crystalline sublimate (20 mg.) as needles, m. p. 107—109° (Found: C, 71·6; H, 6·0%; *M*, 244). Light absorption was similar to that of dimethyl terephthalate but in view of the presence of absorption at 3240 cm.$^{-1}$ (≡CH) this substance was not further investigated.

Oxidative Coupling of Dihex-5-yn-1-yl Terephthalate (Ic; $n = 4$).—A solution of the ester (1 g.) and cupric acetate (3 g.) in pyridine–ether (6 : 1; 700 c.c.) was heated under reflux for 67 hr. The green solution was reduced to small bulk then carefully acidified, and the neutral fraction was chromatographed on alumina. The benzene eluate (350 mg., 35%) proved to be the substantially pure cyclic dimer *bisocta*-3 : 5-*diynylene bisterephthalate* (IIIc; $n = 4$), m. p. 210—211° (from benzene) (Found: C, 74·1; H, 6·5%; *M*, 618. $C_{40}H_{40}O_8$ requires C, 74·2; H, 6·2%; *M*, 648), $\lambda_{max.}$ 242, 285, and 294 mμ (ε 38,000, 3900, and 2900 respectively), $\nu_{max.}$ 2100 and 1720 cm.$^{-1}$. The early fractions yielded, in addition to the dimer, a few needles, m. p. 145—148°, possibly the cyclic monomer (IIc; $n = 4$) ($\lambda_{max.}$ 244, 250, 256, 286, and 294 mμ; ε not determined). The same reaction in pyridine–ether–methanol (3 : 1 : 3) gave a virtually quantitative yield of dimethyl terephthalate, m. p. 142°, together with dodeca-5 : 7-diyne-1 : 12-diol (33% yield), m. p. 47—49°, undepressed on admixture with a genuine specimen (see below).

Dodeca-5 : 7-diyne-1 : 12-diol.—A solution of hex-5-yn-1-ol [9] (2 g.) and cupric acetate (3 g.) in pyridine–methanol (1 : 1, 100 c.c.) was heated under reflux for 7 hr., cooled and carefully added to excess of dilute hydrochloric acid. The solid from an ether extract, on crystallisation from ether–light petroleum, gave the *diol*, m. p. 49—50° (Found: C, 74·4; H, 9·4. $C_{12}H_{18}O_2$ requires C, 74·2; H, 9·3%), $\lambda_{max.}$ 227, 238, and 254 mμ (ε 400, 380, and 230 respectively), $\nu_{max.}$ 2220 and 2130 cm.$^{-1}$.

Diethyl Hepta-1 : 6-diyne-4 : 4-dicarboxylate (V).—Diethyl malonate (27 g.) was added to dry ethanol (150 c.c.) containing sodium ethoxide (from sodium, 7·8 g.). After 5 min., 3-bromoprop-1-yne, n_D^{17} 1·4896 (42 g.), was slowly added to the stirred suspension, and the mixture heated under reflux for 30 min. After removal of the alcohol in a vacuum, the residue was diluted with water, and the neutral fraction isolated and dissolved in light petroleum. The ester (33 g., 82%) slowly separated in octahedra, m. p. 45° (Schulte and Nimke [21] give 45·5°).

Oxidative Coupling of Diethyl Hepta-1 : 6-diyne-4 : 4-dicarboxylate (V).—A solution of the ester (2 g.) and cupric acetate (5 g.) in pyridine–ethanol (1 : 1; 700 c.c.) was set aside for one month, by which time the ethynyl group content had become quite small. The neutral fraction was chromatographed on alumina, being eluted first with benzene (appreciable ethynyl absorption at 3300 cm.$^{-1}$) and then with chloroform. The chloroform eluate, a red oil (1·2 g.), rapidly polymerised (before polymerisation, $\lambda_{max.}$ 226 and 254 mμ; ε 1700 and 732). In one experiment the chloroform eluate was immediately subjected to catalytic hydrogenation (PtO_2). 460 c.c. of hydrogen (calc. for the cyclic dimer, 540 c.c.) were taken up during 21 hr.; the product was an intractable gum.

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THE CHEMISTRY DEPARTMENT, THE UNIVERSITY,
GLASGOW.

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[21] Schulte and Nimke, *Arch. Pharm.*, 1957, **290**, 597.

183. *The Chemotherapy of Schistosomiasis. Part II.* Some Ethers of* p-*Aminophenol.*

By J. N. Ashley, R. F. Collins, M. Davis, and N. E. Sirett.

Some alkyl, *cyclo*alkyl, aralkyl, alkoxyalkyl, and aryloxyalkyl ethers of *p*-aminophenol have been prepared. Many of the compounds are schistosomicides.

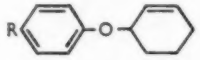
In Part I of this series * we described a series of schistosomicidal aromatic diamines of the general formula p-$NH_2 \cdot C_6H_4 \cdot O \cdot [CH_2]_{3-9} \cdot O \cdot C_6H_4 \cdot NH_2$-$p$, together with some derivatives and analogues. Subsequently it was found that activity was retained by analogues of the foregoing series which contained only one amino-group, and that many simpler ethers of *p*-aminophenol were curative against *S. mansoni* infections in mice.

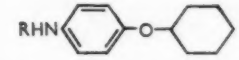
In the present paper we record the preparation of some alkyl, *cyclo*alkyl, aralkyl, alkoxyalkyl, and aryloxyalkyl ethers, together with a few other substituted alkyl ethers required in connection with work on the metabolism of these compounds. The biological results have been published elsewhere.[1] A few compounds of this type have been independently synthesised by The Wellcome Foundation Ltd.,[2] and some others have been adequately described in patent specifications [3] and have therefore been omitted from, or only mentioned briefly in, this paper.

Compounds of the general formula p-$NH_2 \cdot C_6H_4 \cdot OR$ were first studied. *n*-Alkyl and ω-phenylalkyl ethers of *p*-aminophenol were obtained from *p*-nitrophenol and the appropriate bromide according to the general method used in Part I, and the amines were obtained from these by catalytic reduction. Only those derivatives which are new or are inadequately described in the literature are reported here.

Hydrogenation of 3-*p*-nitrophenoxy*cyclo*hexene (I) over palladium–calcium carbonate gave some *p*-aminophenol together with the expected *p*-aminophenoxy*cyclo*hexane (IV). The latter amine was subsequently prepared by Bowden and Green [4] by condensation of *p*-fluoronitrobenzene with potassium *cyclo*hexyl oxide followed by reduction with iron and hydrochloric acid. When, however, the nitro-ether (I) was reduced with iron and acetic acid and the amine was dissolved in hydrochloric acid, the only product isolated was *cyclo*hex-2-enol (as the known phenylurethane). Further investigation showed that the amino-ether (II) initially formed had been hydrolysed by the hydrochloric acid. Acid-

(I): R = NO_2
(II): R = NH_2
(III): R = NHAc





(IV): R = H
(V): R = Ac

hydrolysis of allyl and *cyclo*hexyl ethers is known to be much more rapid at room temperature than that of simple alkyl ethers.[5] Combination of both structural types in the same molecule has obviously led to a compound unstable to acid, in contrast to the acid-stable, saturated ether (IV). Reduction of the nitro-compound (I) using substantially neutral conditions—iron in ethanol containing ferric chloride—yielded (II) in moderate yield. The free base appeared to be stable, but its crystalline hydrochloride decomposed on storage. Its acetyl derivative (III) on reduction over a platinum catalyst gave the saturated acetyl derivative (V), no hydrogenolysis apparently occurring.

The effect on schistosomicidal activity of varying the group R in the series p-$NH_2 \cdot C_6H_4 \cdot O \cdot [CH_2]_5 \cdot OR$ was then studied, and a few lower homologues were also prepared.

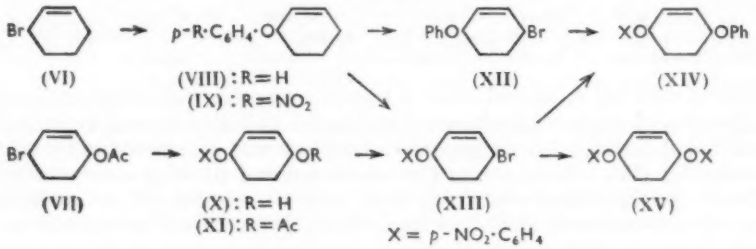
* Part I, Ashley, Collins, Davis, and Sirett, *J.*, 1958, 3298.

[1] Collins, Davis, Edge, and Hill, *Brit. J. Pharmacol.*, 1958, **13**, 238.
[2] The Wellcome Foundation Ltd., B.P. 770,411.
[3] May and Baker Ltd., B.P. 768,144, 770,870.
[4] Bowden and Green, *J.*, 1954, 1797.
[5] Tronow and Ladigina, *Ber.*, 1929, **62**, 2844.

The common intermediates for most of these amines were 3-*p*-nitrophenoxypropyl bromide and 5-*p*-nitrophenoxypentyl bromide. Reaction of these with the appropriate sodium alkoxide gave the methoxy-, ethoxy-, 2-hydroxyethoxy-, 2-methoxyethoxy-, and propoxy-derivatives, respectively. These ethers of *p*-nitrophenol were very susceptible to nucleophilic attack by methoxide ion. Thus, when 3-*p*-nitrophenoxypropyl bromide was treated with excess of sodium methoxide, the principal product was *p*-nitroanisole and some was formed, together with required ether, 1-methoxy-3-*p*-nitrophenoxypropane, even when the theoretical amount of methoxide was used. This procedure failed when applied to benzyl alcohol and it was shown that the benzyl alcohol was partially oxidised by the nitro-group to benzaldehyde, which was isolated as its 2 : 4-dinitrophenylhydrazone. The sodium salt of benzyl alcohol was therefore treated with excess of 1 : 5-dibromopentane to form 5-benzyloxypentyl bromide which was subsequently converted by *p*-nitrophenol into the required ether. The *cyclo*hexyl ether was similarly obtained. Catalytic reduction of all these nitro-compounds proceeded smoothly.

Most of the aryl and heterocyclic ethers were similarly prepared. 1-*p*-Ethoxyphenoxy-5-*p*-nitrophenoxypentane was obtained by alkylation of the available *p*-hydroxyphenoxy-derivative. Some of the *p*-acylaminophenyl ethers were conveniently obtained from 1-*p*-acetamidophenoxy-5-*p*-nitrophenoxypentane by hydrolysis to the amine and subsequent treatment with the acid chloride. The *p*-chloroacetamidophenyl ether with potassium acetate in acetic acid gave the *p*-acetoxyacetamidophenyl derivative, which was partially hydrolysed by dilute sodium hydroxide in cold acetone to the *p*-hydroxyacetamidophenyl ether. The silver salt of 2-hydroxypyridine was employed to make the 2-pyridyl ether since it is known that *N*-alkylation occurs when the sodium salt is used.

Replacement of the central alkane chain of the active diamines by a 1 : 4-linked *cyclo*hexane ring was described in Part I. Since this compound retained schistosomicidal activity, the preparation of a corresponding monoamine was undertaken and was eventually achieved by two different routes. Condensation of crude 3-bromo-6-*p*-nitrophenoxy*cyclo*hexene (XIII), prepared from 3-bromo*cyclo*hexene (VI) *via* 3-*p*-nitrophenoxy*cyclo*hexene (IX) as described in Part I, with potassium phenoxide was unsatisfactory. Since it was not possible to purify this nitro-bromide by distillation, 3-bromo-6-phenoxy*cyclo*hexene (XII) was prepared from 3-phenoxy*cyclo*hexene [6] (VIII) and *N*-bromosuccinimide. This bromide was distilled with only slight decomposition, but on condensation with potassium *p*-nitrophenoxide gave only a low yield of the required product (XIV). An alternative route was therefore examined. 3-Acetoxy-6-bromo*cyclo*hexene [7] (VII) on condensation with



potassium *p*-nitrophenoxide yielded two products, both giving analyses correct for the expected 3-acetoxy-6-*p*-nitrophenoxy*cyclo*hexene (XI), but showing depression of melting points on admixture. The hydroxy-compound (X) corresponding to each isomer was separately treated with phosphorus tribromide and then with potassium *p*-nitrophenoxide to give the same 3 : 6-di-(*p*-nitrophenoxy)*cyclo*hexene (XV) (see Part I). Epimerisation

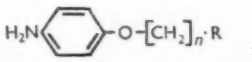
[6] Crossley, *J.*, 1904, 1403; Cornforth, Hughes, and Lions, *J. Proc. Roy. Soc. N.S. Wales*, 1938, **71**, 323.

[7] Ziegler, Spaeth, Schaaf, Schumann, and Winkelmann, *Annalen*, 1942, **551**, 80.

of one isomer probably occurred at the final stage. Condensing the 1-bromo-6-*p*-nitrophenoxy*cyclo*hexene (XIII) obtained from one of the isomeric hydroxy-compounds (X) with potassium phenoxide then gave the mononitro-diether (XIV). Reduction over palladium–calcium carbonate to the saturated amine proceeded normally.

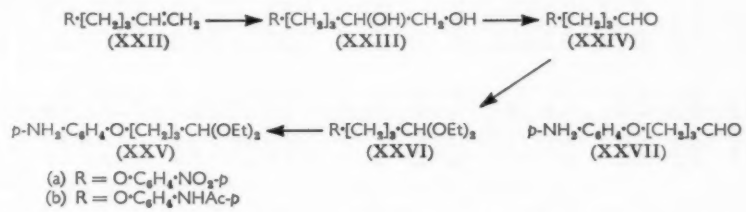
It seemed likely from the biological results [1] that the similar activity found for many different mono- and di-amines derived from *p*-aminophenol might be due to a common active metabolite. A few of the simpler compounds which could be formed by metabolic fission of the polymethylene chain were synthesised but none showed activity *in vivo*.

The primary alcohols (XVI) and (XVII) were obtained by hydrolysis of the corresponding acetates (XVIII) and (XIX), prepared by condensation of the appropriate *p*-nitrophenoxyalkyl bromide with potassium acetate and subsequent catalytic reduction. For



(XVI): $n = 3$, R = OH. (XIX): $n = 5$, R = OAc.
(XVII): $n = 5$, R = OH. (XX): $n = 4$, R = CO_2H.
(XVIII): $n = 3$, R = OAc. (XXI): $n = 5$, R = CO_2H.

the acids (XX) and (XXI), the *p*-nitrophenoxyalkyl bromides were condensed with potassium cyanide and the resulting cyano-compounds were hydrolysed with alkali and then reduced catalytically. When the period of hydrolysis was reduced from 20 to 3 hours, a mixture of the corresponding amide and acid was formed. 6-*p*-Nitrophenoxyhexanoic acid was obtained from the nitrile in higher yield by direct conversion into the methyl ester followed by hydrolysis with potassium hydrogen carbonate; formation of *p*-nitrophenol was thereby minimised. The amides were best obtained by keeping the cyanides in concentrated sulphuric acid and then pouring the solution into water. The nitro-compounds were reduced catalytically.



(XXII) (XXIII) (XXIV)

(XXV) (XXVI) (XXVII)

(a) R = O·C_6H_4·NO_2-*p*
(b) R = O·C_6H_4·NHAc-*p*

The analogous aldehyde diethyl acetal (XXV) was prepared from 5-*p*-nitrophenoxypent-1-ene (XXIIa), which was obtained from potassium *p*-nitrophenoxide and 5-toluene-*p*-sulphonyloxypent-1-ene. An attempt to make compound (XXIIa) by condensation of 5-*p*-nitrophenoxypentyl iodide with trimethylamine and pyrolysis of the corresponding quaternary hydroxide led instead to 1-dimethylamino-5-*p*-nitrophenoxypentane and *p*-nitroanisole. The latter was probably formed by nucleophilic attack of methoxide ion (from the methanol released) at the ether linkage. Refluxing 5-*p*-nitrophenoxypentyl toluene-*p*-sulphonate with pyridine yielded only the quaternary salt. The pentene (XXIIa) was oxidised to the glycol diacetate by iodine and silver acetate [8] and then hydrolysed to the glycol (XXIIIa), which was cleaved quantitatively by periodate to the aldehyde (XXIVa). The corresponding diethyl acetal (XXVIa) was reduced catalytically to the aminoacetal (XXV). Attempts to hydrolyse this acetal to free 4-*p*-aminophenoxybutyraldehyde (XXVII) gave only gums. In the hope that the amino-aldehyde (XXVII) would be more stable under acid conditions, the nitro-glycol (XXIIIa) was reduced and acetylated to give the acetamido-glycol (XXIIIb), which was cleaved with periodate to 5-*p*-acetamidophenoxybutyraldehyde (XXIVb). Acid-hydrolysis gave only an impure salt of the base (XXVII), which could not be purified.

[8] Barkley, Farrar, Knowles, Raffelson, and Thompson, *J. Amer. Chem. Soc.*, 1954, **76**, 5014.

XUM

p-*Aminophenyl ethers*, *p*-$NH_2 \cdot C_6H_4 \cdot O \cdot [CH_2]_n \cdot R$.

n	R	Derivative	Yield (%)	M. p.	Solvent for crystn.	Formula	Found (%) C	Found (%) H	Found (%) N	Required (%) C	Required (%) H	Required (%) N
5	Me	Me·SO_3H	80	196—198° [a]	EtOH–Et_2O	$C_{12}H_{19}ON,CH_4O_3S$	—	—	4·8	—	—	4·8
9	Me	Acetyl	88	90—92 [b]	EtOH	$C_{18}H_{29}O_2N$	—	—	4·6	—	—	4·8
3	$CH{:}CH_2$	Base	85	[c]		$C_{11}H_{15}ON$	74·0	8·4	8·35	74·5	8·5	7·9
		Me·SO_3H		202—203 [d]	MeOH–Et_2O	$C_{11}H_{15}ON,CH_4O_3S$	—	—	5·15	—	—	5·1
3	$CH(OH) \cdot CH_2 \cdot OH$	Base	96	114—116	EtOH	$C_{11}H_{17}O_3N$	62·35	7·4	6·6	62·6	8·1	6·6
3	$CH(OEt)_2$	Base	94	[e]		$C_{14}H_{23}O_3N$	66·4	9·2	5·5	66·4	9·1	5·5
5	$CO \cdot NH_2$	Base	80	141—142	EtOH	$C_{12}H_{16}O_2N_2$	—	—	12·4	—	—	12·6
4	CO_2H	Base	67	173—174 [f]	H_2O	$C_{11}H_{15}O_3N$	—	—	6·6	—	—	6·7
5	CO_2H	Base	81	138	H_2O or EtOH–Pet	$C_{12}H_{17}O_3N$	—	—	6·2	—	—	6·3
2	Ph	Base	74	59	Pet [g]	$C_{14}H_{15}ON$	—	—	6·4	—	—	6·55
		Me·SO_3H		151—152 [h]	EtOH–Et_2O	$C_{14}H_{15}ON,CH_4O_3S$	—	—	4·6	—	—	4·5
3	Ph	Base	85	58—59	Et_2O–Pet	$C_{15}H_{17}ON$	—	—	6·3	—	—	6·15
5	Ph	Acetyl		106	EtOH–H_2O	$C_{19}H_{23}O_2N$	—	—	4·7	—	—	4·7
3	OAc	Base	77	52—54	Et_2O–Pet	$C_{11}H_{15}O_3N$	—	—	6·9	—	—	6·7
5	OAc	Base	95	39	Et_2O–Pet	$C_{13}H_{19}O_3N$	65·6	8·1	5·8	65·8	8·0	5·9
5	OEt	Base	91	[i]		$C_{13}H_{21}O_2N$	70·0	9·4	6·4	69·9	9·5	6·3
		Me·SO_3H		175—177 [j]	EtOH–Et_2O	$C_{13}H_{21}O_2N,CH_4O_3S$	—	—	4·4	—	—	4·4
5	$O \cdot [CH_2] \cdot OMe$	Base	91	—	—	$C_{14}H_{23}O_2N$	66·4	9·05	5·6	66·4	9·1	5·5
		Me·SO_3H		154—156		$C_{14}H_{23}O_2N,CH_4O_3S$	—	—	4·1	—	—	4·0
5	*cyclo*Hexyloxy	Base	87	[k]		$C_{17}H_{27}O_2N$	73·4	9·65	5·05	73·7	9·75	5·05
		Me·SO_3H		145—150	EtOH–Et_2O	$C_{17}H_{27}O_2N,CH_4O_3S$	—	—	3·7	—	—	3·75
5	$O \cdot C_6H_4Me$-*p*	Base	65	61	EtOH	$C_{18}H_{23}O_2N$	75·9	8·0	5·0	75·7	8·1	4·9
5	$O \cdot C_6H_3Me_2$-1 : 3 : 5	Base	63	88—89	Et_2O	$C_{19}H_{25}O_2N$	76·0	8·3	4·7	76·2	8·4	4·7
		Me·SO_3H		[m]		$C_{19}H_{25}O_2N,CH_4O_3S$	—	—	3·8	—	—	3·9
5	$O \cdot C_6H_4Ph$-*p*	Base	90	88—90	Et_2O–Pet	$C_{23}H_{25}O_2N$	—	—	4·1	—	—	3·9
		Me·SO_3H		197—199	EtOH	$C_{23}H_{25}O_2N,CH_4O_3S$	65·3	6·7	3·2	65·0	6·5	3·2
5	$O \cdot C_6H_4 \cdot OH$-*p*	Base	67	108—110 [n]	EtOH–H_2O	$C_{17}H_{21}O_3N$	—	—	4·9	—	—	4·9
		Me·SO_3H	90	155—157		$C_{17}H_{21}O_3N,CH_4O_3S$	—	—	3·65	—	—	3·65
5	$O \cdot C_6H_4 \cdot OMe$-*o*	Base	75	55—56	Et_2O–Pet	$C_{18}H_{23}O_3N$	—	—	4·65	—	—	4·65
5	$O \cdot C_6H_4 \cdot OMe$-*p*	Base	67	64—65	EtOH	$C_{18}H_{23}O_3N$	—	—	4·7	—	—	4·65
5	$O \cdot C_6H_4 \cdot OPh$-*p*	Base	68	64—65	Et_2O–Pet	$C_{23}H_{25}O_3N$	—	—	3·7	—	—	3·8
		Me·SO_3H		195—198 [o]	EtOH	$C_{23}H_{25}O_3N,CH_4O_3S$	63·2	6·5	3·1	63·0	6·3	3·1
5	$O \cdot C_6H_4Cl$-*p*	Base	58	50 [p]	Et_2O–Pet	$C_{17}H_{20}O_2NCl$	—	—	4·5	—	—	4·6
5	$O \cdot C_6H_4 \cdot CO_2Et$-*p*	Base	85	74—76	EtOH	$C_{20}H_{25}O_4N$	69·8	7·6	—	70·0	7·3	—
5	$O \cdot C_6H_4 \cdot NH \cdot CO \cdot CH_2 \cdot OH$-*p*	Base	92	137—138	EtOH	$C_{19}H_{24}O_4N_2$	66·7	7·4	8·0	66·3	7·0	8·1
5	1-$C_{10}H_7 \cdot O$	Me·SO_3H	88	167—170	EtOH	$C_{21}H_{23}O_2N,CH_4O_3S$	—	—	3·4	—	—	3·4
5	2-$C_{10}H_7 \cdot O$	Base	75	54—56	Et_2O	$C_{21}H_{23}O_2N$	—	—	4·2	—	—	4·4
5	6-Quinolyloxy	HCl	75	161—163 [q]	EtOH–Et_2O	$C_{20}H_{22}O_2N_2,2HCl$	—	—	6·85	—	—	7·1
5	2-Pyridyloxy	Base	77	95—96	EtOH	$C_{16}H_{20}O_2N_2$	70·5	7·4	10·15	70·6	7·4	10·3

[a] Found: S, 11·4. Reqd.: S, 11·1%. Base described by Allen and Gates (*Org. Synth.*, Coll. Vol. III, p. 140). [b] Base described by General Aniline and Film Corp. (U.S.P. 2,629,658). [c] B. p. 94°/0·01 mm. Nitro-compound reduced with sodium sulphide. [d] Found: S, 11·9. Reqd.: S, 11·7%. [e] B. p. 130—132°/0·04 mm. [f] Hydrochloride described by Davis, Roberts, and Ross (*J.*, 1955, 893). [g] Pet = light petroleum, b. p. 40—60° (but see footnote [r]). [h] Found: S, 10·2. Reqd.: S, 10·4%. [i] B. p. 140—154°/0·04 mm. [j] Found: S, 10·4. Reqd.: S, 10·0%. [k] B. p. 150—155°/0·06 mm. [l] B. p. 170°/0·3 mm. [m] Found: S, 8·55. Reqd.: S, 8·1%. [n] Nitro-compound described in Part I. [o] Found: S, 6·9. Reqd.: S, 7·0%. [p] Found: Cl, 11·4. Reqd.: Cl, 11·6%. [q] Found: Cl, 18·5. Reqd.: Cl, 18·0%. [r] B. p. 60—80°.

Some earlier attempts to prepare an aldehyde from available intermediates were unsuccessful. Conversion of 6-*p*-nitrophenoxyhexanoyl chloride into the Reissert complex, by using liquid hydrogen cyanide and quinoline,[9] proceeded normally, but hydrolysis then resulted in recovery of the acid. α-Bromination of 6-*p*-nitrophenoxyhexanoic acid was also tried since the corresponding α-hydroxy-acid could probably be cleaved with lead tetra-acetate to an aldehyde.[10] However, treating the acid with bromine containing some phosphorus tribromide led to nuclear bromination. Oxidation of 5-*p*-nitrophenoxypentanol with the theoretical amount of chromic acid yielded the ester, 5-*p*-nitrophenoxypentyl 5-*p*-nitrophenoxypentanoate, formed by oxidation of some of the alcohol to the carboxylic acid and subsequent esterification with the starting material.[11]

Experimental

Light petroleum refers, unless otherwise stated, to the fraction of b. p. 40—60°.

The following compounds were prepared by condensation of potassium *p*-nitrophenoxide with the appropriate bromide: 1-p-*nitrophenoxydecane* (67%), m. p. 57—58° (from aqueous acid) (Found: N, 4·9. $C_{16}H_{25}O_3N$ requires N, 5·0%); 1-p-*nitrophenoxy*-3-*phenylpropane* (78%), m. p. 80·5—81·5° (from ethanol) (Found: N, 5·6. $C_{15}H_{15}O_3N$ requires N, 5·5%).

The following 5-substituted 1-p-*nitrophenoxypentanes* were prepared (except where otherwise stated) by condensation of 5-*p*-nitrophenoxypentyl bromide with the appropriate phenol (using 1 equiv. of alkali) or alcohol (using 1 equiv. of sodium): *ethoxy*- (70%), b. p. 165—176°/0·2 mm. (Found: N, 5·75. $C_{13}H_{19}O_4N$ requires N, 5·55%); 2′-*methoxyethoxy*- (67%), b. p. 165—170°/0·05 mm. (Found: C, 59·65; H, 7·3; N, 5·0. $C_{14}H_{21}O_5N$ requires C, 59·4; H, 7·4; N, 4·95%); (3 : 5-*dimethylphenoxy*)- (77%), m. p. 74° (from ethanol) (Found: C, 69·2; H, 6·9; N, 4·5. $C_{19}H_{23}O_4N$ requires C, 69·3; H, 7·0; N, 4·3%); p-*phenylphenoxypentane* (66%), m. p. 97—98° (from ethanol) (Found: C, 73·3; H, 6·25; N, 3·9. $C_{23}H_{23}O_4N$ requires C, 73·2; H, 6·1; N, 3·7%); o-*methoxyphenoxy*- (35%; from 5-guaiacyloxypentyl bromide), m. p. 54—56° (from ethanol) (Found: N, 4·35. $C_{18}H_{21}O_5N$ requires N, 4·2%); p-*phenoxyphenoxy*- (48%), m. p. 86—87° (from ether) (Found: C, 70·3; H, 5·8; N, 3·7. $C_{23}H_{23}O_5N$ requires C, 70·2; H, 5·9; N, 3·6%); 1′-*naphthyloxy*- (59%), m. p. 99—100° (from benzene–light petroleum) (Found: N, 3·8. $C_{21}H_{21}O_4N$ requires N, 4·0%); 2′-*naphthyloxy*- (70%), m. p. 93—94° (from ethanol) (Found: N, 4·25. $C_{21}H_{21}O_4N$ requires N, 4·0%); and 6′-*quinolyloxy*- (45%), m. p. 115—117° (from benzene–light petroleum) (Found: N, 7·5. $C_{20}H_{20}O_4N_2$ requires N, 7·95%).

5-*Toluene*-p-*sulphonyloxypentene*.—Toluene-*p*-sulphonyl chloride (55 g.) was added during 30 min. to a stirred mixture of 1-hydroxypent-4-ene [12] (22 g.) and dry pyridine (120 ml.) below 20°. After a further 1 hr. the mixture was poured on ice and extracted with chloroform, and the washed and dried extract was distilled, yielding the *ester* (56 g., 91%), b. p. 122—126°/0·03 mm. (Found C, 59·8; H, 6·8; S, 13·8. $C_{12}H_{16}O_3S$ requires C, 60·0; H, 6·7; S, 13·3%). Condensation with potassium *p*-nitrophenoxide gave 5-p-*nitrophenoxypentene* (80%), b. p. 126°/0·04 mm. (Found: N, 7·0. $C_{11}H_{13}O_3N$ requires N, 6·8%).

5-p-*Nitrophenoxypentane*-1 : 2-*diol*.—Iodine (9·9 g.) was added during 15 min. to a stirred suspension of silver acetate (15 g.) in acetic acid (250 ml.) and water (0·7 ml.) containing 5-*p*-nitrophenoxypentene (8·1 g.). After 1 hr. at 20—25°, the mixture was heated at 90—95° for 3 hr., filtered, and concentrated to low bulk. Methanol (200 ml.) was added and the filtered solution was treated with potassium hydroxide (until just alkaline), and a solution of potassium hydrogen carbonate (8 g.) in water (40 ml.) was added. The whole was then refluxed for 3 hr., solvent was distilled off, water was added, and the mixture was extracted with chloroform. The dried extract was evaporated and the residue crystallised from ethyl acetate–light petroleum, yielding the *diol* (7·9 g., 85%), m. p. 68—69° (Found: C, 54·9; H, 6·4; N, 6·15. $C_{11}H_{15}O_5N$ requires C, 54·7; H, 6·2; N, 5·8%).

5-p-*Acetamidophenoxypentane*-1 : 2-*diol*.—A mixture of 5-*p*-aminophenoxypentane-1 : 2-diol (2·8 g.), acetic anhydride (10 g.), and pyridine (30 ml.) was heated on the steam-bath, then

[9] Grosheintz and Fischer, *J. Amer. Chem. Soc.*, 1941, **63**, 2021.
[10] Jackson, *Organic Reactions*, 1944, **2**, 345.
[11] Rodd, "Chemistry of Carbon Compounds," Elsevier, London, 1951, Vol. IA, p. 462.
[12] Gaubert, Linstead, and Rydon, *J.*, 1937, 1972.

immediately poured into water. The solid product was refluxed for 2 hr. with potassium hydrogen carbonate (3 g.) in water (15 ml.) and sufficient methanol to give a clear solution. The solvent was then distilled off, water was added, and the mixture was extracted with chloroform and with ethyl acetate. The combined extracts were dried and evaporated, and the residue was crystallised from ethyl acetate, giving the *diol* (1·9 g.), m. p. 96—98° (softens at 92°) (Found: C, 61·85; H, 7·8; N, 5·5. $C_{13}H_{19}O_4N$ requires C, 61·6; H, 7·5; N, 5·5%).

4-p-*Acetamidophenoxybutyraldehyde*.—0·05N-Sodium metaperiodate (13·2 ml.) was added rapidly to a solution of 5-*p*-acetamidophenoxypentane-1 : 2-diol (1·6 g.) in methanol (20 ml.) cooled to 0°. The solution was kept overnight at room temperature, then filtered, and the filtrate was evaporated *in vacuo*. Water was added and the product was extracted into chloroform. Evaporation of the extract and crystallisation of the residue from ethyl acetate–light petroleum (b. p. 60—80°) gave the *aldehyde* (1 g.), m. p. 87—88° (Found: C, 65·5; H, 7·2; N, 6·4. $C_{13}H_{15}O_3N$ requires C, 65·2; H, 6·8; N, 6·3%).

4-p-*Nitrophenoxybutyraldehyde* was similarly prepared (96%) and had m. p. 76—77° (Found: C, 57·6; H, 5·6; N, 6·7. $C_{10}H_{11}O_4N$ requires C, 57·5; H, 5·3; N, 6·7%). A mixture of the aldehyde (9·7 g.), redistilled ethyl orthoformate (6·9 g., 7·8 ml.), concentrated hydrochloric acid (0·04 ml.), and dry ethanol (50 ml.) was kept at room temperature for 24 hr., refluxed for 10 min., made just alkaline with ethanolic potassium hydroxide, and concentrated. The residue was extracted with ether, and the washed and dried extract was distilled, yielding the *diethyl acetal* (12·8 g.), b. p. 142—145°/0·03 mm. (Found: C, 59·3; H, 7·4; N, 4·9. $C_{14}H_{21}O_5N$ requires C, 59·4; H, 7·4; N, 4·95%).

3-p-*Nitrophenoxypropyl Cyanide*.—3-*p*-Nitrophenoxypropyl bromide (5·2 g.) was added to a solution of potassium cyanide (1·43 g., 1·1 mol.) in water (5 ml.) and ethanol (50 ml.), and the mixture was boiled for 4 hr., then evaporated. The residue was treated with water and extracted with ether. The extract was washed, dried, and evaporated, the residue was triturated with light petroleum and filtered, and the product was crystallised from ether, yielding the *cyanide* (46%), m. p. 50—52° (Found: N, 13·2. $C_{10}H_{10}O_3N_2$ requires N, 13·6%).

4-p-*Nitrophenoxybutyl cyanide*, similarly obtained, and purified by chromatography in benzene–light petroleum over alumina and recrystallisation from ether, had m. p. 35—36° (Found: N, 12·7. $C_{11}H_{12}O_3N_2$ requires N, 12·7%).

5-p-*Nitrophenoxypentyl cyanide* was similarly prepared, but was distilled, and the fraction, b. p. 200—210°/0·02 mm. (34·6 g., 74%), was recrystallised from ether, giving the cyanide, m. p. 38—39° (Found: N, 12·1. $C_{12}H_{14}O_3N_2$ requires N, 12·0%).

5-p-*Nitrophenoxypentanoic Acid*.—Crude 4-*p*-nitrophenoxybutyl cyanide (prepared from 54·8 g. of bromide) was hydrolysed by refluxing 2N-sodium hydroxide (150 ml.) and ethanol (150 ml.) overnight. The product recrystallised from aqueous methanol and from benzene, giving 5-p-*nitrophenoxypentanoic acid* (25·7 g., 54%) in needles, m. p. 98—100° (Found: N, 6·2. $C_{11}H_{13}O_5N$ requires N, 5·9%).

4-p-*Nitrophenoxybutane*-1-*carboxyamide*.—From an experiment similar to the above, but with refluxing for only 3 hr., there were obtained 19·65 g. (41%) of the foregoing acid together with 7·8 g. (16%) of the intermediate *amide*, m. p. 108—112°. Recrystallisation of the latter from benzene gave sparingly soluble prisms, m. p. 117—118° (Found: N, 11·6. $C_{11}H_{14}O_4N_2$ requires N, 11·8%).

6-p-*Nitrophenoxyhexanoic Acid*.—(*a*) Crude 5-*p*-nitrophenoxypentyl cyanide (from 28·8 g. of bromide) was hydrolysed as described for the lower homologue. Crystallisation of the product from benzene gave 6-*p*-*nitrophenoxyhexanoic acid* (9·65 g. 38%) in prisms, m. p. 101—103° (Found: N, 5·8. $C_{12}H_{15}O_5N$ requires N, 5·5%). (*b*) Dry hydrogen chloride was passed for 2 hr. into a refluxing mixture of 5-*p*-nitrophenoxypentyl cyanide (40 g.), methanol (200 ml.), and water (3·1 g.). Solvent was removed, water was added to the residue, and the solid was filtered off and recrystallised from ethanol, yielding the *methyl ester* (30 g., 66%), m. p. 85—86° (Found: C, 58·0; H, 6·4; N, 5·3. $C_{13}H_{17}O_5N$ requires C, 58·4; H, 6·4; N, 5·2%). Hydrolysis with potassium hydrogen carbonate in boiling aqueous methanol yielded the acid (65%), m. p. 104—105°, together with some unhydrolysed ester (28%). The acid chloride, prepared by using thionyl chloride, was converted directly into the *N-methylanilide*, m. p. 89—90° (from light petroleum, b. p. 100—120°) (Found: C, 66·5; H, 6·25; N, 8·4. $C_{19}H_{22}O_4N_2$ requires C, 66·6; H, 6·4; N, 8·2%).

5-p-*Nitrophenoxypentane*-1-*carboxyamide*.—A mixture of 5-*p*-nitrophenoxypentyl cyanide (29·3 g.) and concentrated sulphuric acid (10 ml.) was kept at room temperature for 24 hr.,

then treated with ice and 2N-sodium hydroxide. The product was filtered off, washed, dried and crystallised from benzene and from chloroform–light petroleum, giving 5-p-*nitrophenoxypentane*-1-*carboxyamide* (17·0 g., 54%), in needles, m. p. 127—129° (Found: N, 11·2. $C_{12}H_{16}O_4N_2$ requires N, 11·1%).

3-p-*Nitrophenoxypropyl Acetate*.—3-*p*-Nitrophenoxypropyl bromide (52 g.) and potassium acetate (52 g.) in acetic acid (100 ml.) were heated under reflux for 1·5 hr., and the mixture then poured into water. The solid was crystallised from ethanol, giving the *acetate* (42·1 g., 88%), m. p. 63—65° (Found: N, 6·0. $C_{11}H_{13}O_5N$ requires N, 5·9%).

5-p-*Nitrophenoxypentyl acetate* was similarly prepared (92%) and had m. p. 72° (Found: C, 58·5; H, 5·9; N, 5·4. $C_{13}H_{17}O_5N$ requires C, 58·5; H, 6·4; N, 5·2%).

5-p-*Nitrophenoxypentan*-1-*ol*.—5-*p*-Nitrophenoxypentyl acetate (20 g.) was stirred and heated with 2N-hydrochloric acid (150 ml.) at 100° for 24 hr. The product was extracted into ether, the extract was dried and evaporated, and the residue was triturated with methanol; the insoluble portion was unchanged ester (3 g.; m. p. 65—68°). The solution was evaporated and the residue repeatedly extracted with light petroleum (b. p. 60—80°). Evaporation of the extract gave 5-p-*nitrophenoxypentan*-1-*ol* (11 g., 77%), m. p. 33—35° (Found: C, 58·9; H, 6·9; N, 6·1. $C_{11}H_{15}O_4N$ requires C, 58·7; H, 6·7; N, 6·2%).

5-p-*Nitrophenoxypentyl* 5-p-*Nitrophenoxypentanoate*.—A solution of chromium trioxide (3·1 g.) in 80% acetic acid (24 ml.) was added during 1 hr. to a solution of 5-*p*-nitrophenoxypentan-1-ol (10·3 g.) in acetic acid (50 ml.). After a further 2 hr. the acetic acid was distilled off and the residue was treated with water and extracted with chloroform. The washed and dried extract was evaporated and the residue was crystallised from ethanol, giving the *ester* (2·3 g.), m. p. 84—86°, raised by recrystallisation from acetic acid to 92—93° (Found: C, 59·2; H, 5·6; N, 6·4%; *M*, 480. $C_{22}H_{26}O_8N_2$ requires C, 59·2; H, 5·8; N, 6·3%; *M*, 446).

1-*Dimethylamino*-5-p-*nitrophenoxypentane*.—A mixture of 5-*p*-nitrophenoxypentyl bromide (14·4 g.) and 25% w/w ethanolic dimethylamine (48 ml., 4 mol.) was heated for 24 hr. at 100° in a sealed tube. The solution was concentrated, basified, and extracted with chloroform. The extract was washed, dried, and distilled, giving 1-*dimethylamino*-5-p-*nitrophenoxypentane* (6·1 g., 49%), b. p. 150—155°/0·01 mm. (with partial decomp.), m. p. 34—35° (Found: N, 10·95. $C_{13}H_{20}O_3N_2$ requires N, 11·1%). The *picrate* had m. p. 125—127° (Found: N, 14·6. $C_{13}H_{20}O_3N_2,C_6H_3O_7N_3$ requires N, 14·6%).

5-p-*Nitrophenoxypentyl iodide* was prepared from the corresponding bromide with sodium iodide in acetone in 89% yield (Found: I, 37·9. $C_{11}H_{14}O_3NI$ requires I, 37·9%).

Trimethyl-5-p-*nitrophenoxypentylammonium Iodide*.—A mixture of the foregoing iodide (52·5 g.) and 33% ethanolic trimethylamine (200 ml.) was refluxed for 1 hr., cooled, and diluted with ether, giving the quaternary *salt* (54 g.), m. p. 134—135° (Found: N, 6·7; I, 32·2. $C_{14}H_{23}O_3N_2I$ requires N, 7·1; I, 32·2%).

Pyrolysis of Trimethyl-5-p-*nitrophenoxypentylammonium Hydroxide*.—The foregoing salt (52 g.) in water (250 ml.) was shaken with freshly precipitated silver oxide (from 32 g. of silver nitrate) for 2 hr. The mixture was filtered and the filtrate was evaporated. The residue was pyrolysed and distilled at 110—140°/0·1 mm. The distillate was dissolved in ether, extracted with 2N-hydrochloric acid, washed, dried, and evaporated. The residue (13·5 g., 49·5%) was *p*-nitroanisole (Found: C, 55·25; H, 5·1; N, 9·2. Calc. for $C_7H_7O_3N$: C, 55·0; H, 4·6; N, 9·15%), identified by comparison with an authentic specimen. The acid extract was basified and extracted with ether. Distillation of the extract gave 1-dimethylamino-5-*p*-nitrophenoxypentane (5 g.), b. p. 155°/0·01 mm. The picrate had m. p. 123—126°, not depressed by an authentic specimen.

1-p-*Nitrophenoxy*-5-*toluene*-p-*sulphonyloxypentane*.—5-*p*-Nitrophenoxypentanol (prepared from 10 g. of the acetate) was treated with toluene-*p*-sulphonyl chloride (10 g.) in pyridine (30 ml.) at 0°, yielding the *ester* (7·2 g., 51%), m. p. 62—63° (Found: C, 57·15; H, 5·7; N, 3·7. $C_{18}H_{21}O_6NS$ requires C, 57·0; H, 5·55; N, 3·7%). When refluxed for 6 hr. with pyridine, this ester gave the quaternary *pyridinium toluene*-p-*sulphonate* m. p. 137—138° (Found: N, 6·0. $C_{23}H_{26}O_6N_2S$ requires N, 6·1%).

3-p-*Aminophenoxypropan*-1-*ol*.—1-Acetoxy-3-*p*-aminophenoxypropane (14·6 g.) was dissolved in 2N-hydrochloric acid (100 ml.), and the solution was kept for 2 days, then basified with 50% aqueous sodium hydroxide. 3-p-*Aminophenoxypropan*-1-*ol* (10·5 g., 90%), after recrystallisation from chloroform, had m. p. 90—92° (Found: N, 8·3. $C_9H_{13}O_2N$ requires N, 8·4%). The *methanesulphonate* had m. p. 169—171° (Found: N, 5·4. $C_9H_{13}O_2N,CH_4O_3S$ requires N, 5·3%).

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5-p-*Aminophenoxypentan*-1-*ol* was similarly prepared (92%) and had m. p. 93° (Found: C, 67·7; H, 8·9; N, 7·2. $C_{11}H_{17}O_2N$ requires C, 67·7; H, 8·7; N, 7·2%).

5-p-*Acetamidophenoxypentan*-1-*ol*.—(*a*) A mixture of 1-*p*-acetamidophenoxy-5-acetoxypentane (6·7 g.), potassium hydrogen carbonate (6·7 g.), methanol (150 ml.), and water (20 ml.) was refluxed for 2 hr., concentrated, and diluted with water. The product was extracted into chloroform, the extract was dried and concentrated, and the residue was recrystallised from toluene, giving the *alcohol* (4·5 g.), m. p. 113—115° (Found: C, 66·0; H, 8·2; N, 5·9. $C_{13}H_{19}O_3N$ requires C, 65·8; H, 8·0; N, 5·9%). (*b*) The same compound, m. p. 113—115°, was obtained from 5-*p*-aminophenoxypentan-1-ol by treatment with an excess of acetic anhydride in aqueous sodium hydrogen carbonate.

3-p-*Aminophenoxy*cyclo*hexene*.—A mixture of 3-*p*-nitrophenoxy*cyclo*hexene (see Part I) (8 g.), reduced iron powder (8 g.), and anhydrous ferric chloride (2 g.) in ethanol (200 ml.) and water (2 ml.) was stirred and refluxed overnight, then cooled and filtered through "Celite." The filtrate was evaporated *in vacuo*, the residue was dissolved in ether, and the solution was rapidly washed with N-sodium hydroxide and extracted 7 times with 2N-acetic acid. The acid extracts were basified with sodium carbonate, the product was extracted into ether, and the extract was washed, dried, and evaporated. Distillation of the residue afforded 3-p-*aminophenoxy*cyclo*hexene* (3·4 g., 49%), b. p. 120—122°/0·3 mm. (Found: C, 76·0; H, 8·2; N, 7·4. $C_{12}H_{15}ON$ requires C, 76·2; H, 7·9; N, 7·4%). The *acetyl derivative* had m. p. 127° (Found: C, 72·7; H, 7·2; N, 6·1. $C_{14}H_{17}O_2N$ requires C, 72·7; H, 7·35; N, 6·1%).

p-*Aminophenoxy*cyclo*hexane*.—3-*p*-Nitrophenoxy*cyclo*hexene (30 g.) in methanol (500 ml.) was reduced over 1% palladium–calcium carbonate (10 g.). The filtered solution was evaporated *in vacuo* and the residue was dissolved in ether and filtered from *p*-aminophenol (3·4 g.). The ethereal solution was washed with 2N-sodium hydroxide and water and extracted with 2N-hydrochloric acid. The acid extract was made alkaline, the base was taken up in ether, and the ether solution was dried and evaporated. Distillation of the residue gave p-*aminophenoxy*cyclo*hexane* (16 g., 62%), b. p. 101—102°/0·05 mm. (Found: C, 75·1; H, 9·1; N, 7·15. $C_{12}H_{17}ON$ requires C, 75·4; H, 8·9; N, 7·3%). The base formed a *methanesulphonate* (Found: N, 5·05; S, 11·5. $C_{12}H_{17}ON,CH_4O_3S$ requires N, 4·9; S, 11·15%).

The acetyl derivative, m. p. 154—155° (lit.,[3] 155°), was identical with a specimen, m. p. 154°, obtained by catalytic reduction of 3-*p*-acetamidophenoxy*cyclo*hexene over platinum oxide in ethanol.

3-*Acetoxy*-6-p-*nitrophenoxy*cyclo*hexene*.—A mixture of 3-acetoxy-6-bromo*cyclo*hexene [7] (12·2 g.) and potassium *p*-nitrophenoxide (15 g.) in dry acetone (100 ml.) was refluxed for 18 hr. and filtered hot, and the filtrate was concentrated and treated with ether. The ethereal solution was washed with dilute alkali and water, dried, and evaporated, and the residue was triturated thrice with warm light petroleum. The insoluble residue was combined with some solid which separated gradually from the light petroleum washings, and crystallised twice from methanol, giving the *isomer* A (2·15 g.) in prismatic needles, m. p. 117—118° (Found: C, 60·9; H, 5·7; N, 5·4. $C_{14}H_{15}O_5N$ requires C, 60·7; H, 5·4; N, 5·1%). Evaporation of the light petroleum and methanol solutions gave a low-melting solid (2·2 g.) which was dissolved in benzene–light petroleum (b. p. 80—100°) and chromatographed over alumina. Recrystallisation of the product from methanol gave the pure *isomer* B, m. p. 65° (Found: C, 60·8; H, 5·4; N, 5·4%).

4-p-*Nitrophenoxy*cyclo*hex*-2-*enol*.—(*a*) The preceding acetoxy-compound A (0·5 g.) was refluxed with potassium hydrogen carbonate (0·6 g.) in water (5 ml.) and methanol (30 ml.) for 1·5 hr. After distillation of the methanol, the residue was treated with water, and the product filtered off and recrystallised from ethanol, giving 4-p-*nitrophenoxy*cyclo*hex*-2-*enol*, *isomer* A (0·4 g.), m. p. 89—90° (Found: C, 61·0; H, 5·4; N, 6·1. $C_{12}H_{13}O_4N$ requires C, 61·3; H, 5·5; N, 6·0%). (*b*) Similar hydrolysis of the acetate isomer B (6·65 g.) yielded 4-p-*nitrophenoxy*-cyclo*hex*-2-*enol*, *isomer* B (5·35 g.; m. p. 65—70°) which on recrystallisation from methanol gave first some 3 : 6-di-(*p*-nitrophenoxy)*cyclo*hexene (0·15 g.; m. p. 165—166°; present as impurity in the B-acetate). Dilution of the mother-liquors with water gave the *hydroxy-compound*, *isomer* B (4·8 g.) which after recrystallisation from ether–light petroleum had m. p. 87—88° (Found: C, 61·2; H, 5·5; N, 6·0%), depressed to 70—76° on admixture with isomer A.

3-*Bromo*-6-p-*nitrophenoxy*cyclo*hexene*.—(*a*) Phosphorus tribromide (1 g.) in dry benzene (5 ml.) was slowly added to a stirred suspension of the hydroxy-compound A (2 g.) in dry benzene (20 ml.) at 10—20°. The mixture was stirred overnight, then poured on ice. The product was extracted into ether, and the extract was washed, dried, and evaporated. The oily product

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was condensed with potassium *p*-nitrophenoxide and yielded 3 : 6-di-(*p*-nitrophenoxy)*cyclo*hexene, m. p. 171°, identical with a specimen previously prepared (see Part I). (*b*) The bromo-compound B was similarly prepared from the hydroxy-compound B. On reaction with potassium *p*-nitrophenoxide it afforded the same product, m. p. 164—166°, mixed m. p. 169—170°.

3-*Bromo*-6-*phenoxy*cyclo*hexene*.—A mixture of 3-phenoxy*cyclo*hexene [6] (42 g.), *N*-bromosuccinimide (43 g.), and dry benzoyl peroxide (0·1 g.) in dry carbon tetrachloride (300 ml.) was refluxed for 1 hr., cooled, filtered, concentrated, and distilled. The fraction (20 g.) of b. p. 90—110°/0·3 mm. was redistilled, giving 3-*bromo*-6-*phenoxy*cyclo*hexene* (6·2 g.), b. p. 100°/0·3 mm. (Found: C, 56·1; H, 5·2; Br, 32·4. $C_{12}H_{13}OBr$ requires C, 56·95; H, 5·1; Br, 31·6%).

3-p-*Nitrophenoxy*-6-*phenoxy*cyclo*hexene*.—(*a*) A mixture of 3-bromo-6-*p*-nitrophenoxy*cyclo*hexene (prepared from 33·2 g. of hydroxy-compound, isomer A) and potassium phenoxide (33·1 g.) in dry acetone (500 ml.) was refluxed for 6 hr., then concentrated, and the residue was treated with water. The product was filtered off and recrystallised from acetic acid, giving 3-p-*nitrophenoxy*-6-*phenoxy*cyclo*hexene* (25·2 g., 57% from hydroxy-compound), m. p. 125—126°. (*b*) A similar condensation between 3-*bromo*-6-*phenoxy*cyclo*hexene* (6·2 g.) and potassium *p*-nitrophenoxide (6·2 g.) gave the same product (0·25 g.), m. p. 126° (Found: C, 69·6; H, 5·7; N, 5·0. $C_{18}H_{17}O_4N$ requires C, 69·45; H, 5·5; N, 4·5%).

Catalytic reduction over 1% palladium–calcium carbonate in methanol yielded 1-p-*amino*-*phenoxy*-4-*phenoxy*cyclo*hexane* (72%), m. p. 118—119° (from methanol) (Found: C, 76·6; H, 7·4; N, 5·1. $C_{18}H_{21}O_2N$ requires C, 76·4; H, 7·4; N, 5·0%).

1-*Methoxy*-3-p-*nitrophenoxypropane*.—3-*p*-Nitrophenoxypropyl bromide (26 g.) was added to a solution of sodium (2·3 g.) in methanol (100 ml.), and the solution was refluxed overnight, concentrated, diluted with water, and extracted with ether. The washed and dried ether solution was distilled. Some *p*-nitroanisole distilled first, followed by crude 1-methoxy-3-*p*-nitrophenoxypropane (14·75 g., 70%), b. p. 120—140°/0·3 mm. Redistillation gave the pure *nitro-compound*, b. p. 127—130°/0·1 mm., m. p. 35—36° (Found: N, 6·7. $C_{10}H_{13}O_4N$ requires N, 6·6%). When a similar experiment was carried out using 4·6 g. (2 equiv.) of sodium, the principal product, which separated crystalline on pouring of the solution into water, was *p*-nitroanisole (8·3 g., 54%), m. p. and mixed m. p. 52—53° (Found: C, 55·3; H, 4·7; N, 9·0. Calc. for $C_7H_7O_3N$: C, 55·0; H, 4·6; N, 9·15%).

1-p-*Aminomethylphenoxy*-5-p-*aminophenoxypentane*.—1-*p*-Cyanophenoxy-5-*p*-nitrophenoxypentane (35·7 g.) was reduced catalytically in two stages, (*a*) over 2% of platinum oxide in ethanol and (*b*) over 10% of Raney nickel in ethanolic ammonia at 100°/500 lb. per sq. in. The filtered solution was evaporated, and the residue in ethanol (400 ml.) treated with methanesulphonic acid (20 g.), cooled, and filtered. The *dimethanesulphonate* (52%) crystallised from ethanol in plates, m. p. 208—210° (Found: N, 5·6; S, 13·1. $C_{19}H_{24}O_2N_2,2CH_4O_3S$ requires N, 5·7; S, 13·0%). The base partially decomposed on attempted distillation.

The second stage of the reduction was also effected less satisfactorily with lithium aluminium hydride.

5-cyclo*Hexyloxypentyl Bromide*.—*cyclo*Hexanol (64 g.) was added slowly (40 min.) to a stirred, refluxing suspension of powdered sodamide (25 g.) in dry toluene (500 ml.). After a further 1·5 hr. when evolution of ammonia had ceased, the mixture was cooled, 1 : 5-dibromopentane (300 g.) was added, and the suspension was slowly reheated until a vigorous exothermic reaction occurred. When this had moderated (15 min.), heating and stirring were continued for 20 hr. The filtered solution was then washed with water, dried, and distilled. The fraction (90 g.) of b. p. 130—145°/12 mm. was redistilled, giving the *bromide* (58·4 g., 37%), b. p. 135—140°/12 mm. (Found: Br, 30·95. $C_{11}H_{21}OBr$ requires Br, 32·1%).

1-p-*Aminophenoxy*-5-p-*carboxyphenoxypentane*.—A solution of 1-*p*-aminophenoxy-5-*p*-ethoxycarbonylphenoxypentane (2 g.) in water (20 ml.) and concentrated hydrochloric acid (20 ml.) was boiled for 2·25 hr., then cooled and filtered. The *hydrochloride* (2·0 g., 98%) was recrystallised from very dilute hydrochloric acid, and had m. p. 215—220° (decomp.) (Found: C, 61·5; H, 6·65; N, 4·0; Cl, 10·0. $C_{18}H_{21}O_4N,HCl$ requires C, 61·4; H, 6·25; H, 4·0; Cl, 10·1%).

1-p-*Chloroacetamidophenoxy*-5-p-*nitrophenoxypentane*.—Chloroacetyl chloride (58 ml.) was added in one portion to a rapidly stirred solution of 1-*p*-aminophenoxy-5-*p*-nitrophenoxypentane (58 g.) in water (700 ml.) and methanesulphonic acid (18·5 ml.), cooled in ice. After

10 min. the product was filtered off, washed, and crystallised from ethanol, yielding the *chloroacetamide* (66·8 g., 93%), m. p. 126—127° (Found: C, 57·8; H, 5·05; Cl, 8·85. $C_{19}H_{21}O_5N_2Cl$ requires C, 58·1; H, 5·35; Cl, 9·05%).

1-p-*Acetoxyacetamidophenoxy*-5-p-*nitrophenoxypentane*.—A mixture of the above chloroacetamide (64 g.) and potassium acetate (64 g.) in acetic acid (200 ml.) was stirred and refluxed for 6 hr., then concentrated until the temperature of the liquid reached 130°. The solution was cooled and diluted with water, and the product was filtered off and recrystallised from ethanol, giving the *acetoxyacetamide* (81%), m. p. 118—119° (Found: C, 60·8; H, 5·9; N, 6·7. $C_{21}H_{24}O_7N_2$ requires C, 60·6; H, 5·8; N, 6·7%).

1-p-*Hydroxyacetamidophenoxy*-5-p-*nitrophenoxypentane*.—A mixture of the above acetoxyacetamide (53 g.) and N-sodium hydroxide (138 ml.) in acetone (1·4 l.) was kept at room temperature for 24 hr., then acidified with acetic acid and evaporated. The residue was treated with water, and the solid product recrystallised from aqueous acetic acid, yielding the *hydroxyacetamide* (93%), m. p. 120—121° (Found: C, 61·0; H, 5·8; N, 7·7. $C_{19}H_{22}O_6N_2$ requires C, 61·0; H, 5·9; N, 7·5%).

1-p-*Nitrophenoxy*-5-*pyrid*-2′-*yloxypentane*.—A mixture of 2-hydroxypyridine silver salt (5·4 g.) (dried over P_2O_5) and 1-iodo-5-*p*-nitrophenoxypentane (9·4 g.) (dried over P_2O_5) in dry dioxan (150 ml.) (distilled from sodium) was refluxed for 20 hr., then filtered, and the solid was washed with warm dioxan. The filtrate was concentrated *in vacuo* and the residue recrystallised from methanol, giving 1-p-*nitrophenoxy*-5-*pyrid*-2′-*yloxypentane* (73%), m. p. 97—98° (Found: C, 63·3; H, 6·2; N, 9·0. $C_{16}H_{18}O_4N_2$ requires C, 63·6; H, 6·0; N, 9·3%).

1-p-(2-*Diethylaminoethylamino*)*phenoxy*-5-*phenoxypentane*.—An intimate mixture of 1-*p*-aminophenoxy-5-phenoxypentane (62 g.) and 2-diethylaminoethyl chloride hydrochloride (68·4 g.) was heated at 135° for 20 hr. The product was dissolved in warm water, and the solution was basified with 50% aqueous sodium hydroxide and extracted with ether (3 × 600 ml.). The combined extracts were washed, dried, and evaporated and the residue was distilled. The fraction (33 g., 39%) of b. p. 225—240°/0·2 mm., which gave only a slight diazo-reaction, was twice redistilled, giving the pure *base*, b. p .208—212°/0·08 mm. (Found: C, 74·7; H, 9·5; N, 7·6. $C_{23}H_{34}O_2N_2$ requires C, 74·5; H, 9·2; N, 7·6%).

1-p-[*Bis*-(2-*diethylaminoethyl*)*amino*]*phenoxy*-5-*phenoxypentane*.—To the foregoing mono-(diethylaminoethyl) compound (70 g. crude, containing about 25% of the required bis-condensation product) in toluene (dried over $NaNH_2$) were added powdered sodamide (8·7 g.) and a solution of 2-diethylaminoethyl chloride (from 29·6 g. of hydrochloride treated with aqueous potassium carbonate and extracted into toluene). The stirred mixture was heated slowly to 70°; evolution of ammonia began, and the mixture was finally refluxed for 3·5 hr., then cooled and cautiously diluted with water. The washed and dried toluene solution was distilled and the fraction of b. p. >220°/0·05 mm. was redistilled. The pure *base* was collected at 225—230°/0·05 mm. (Found: C, 74·3; H, 10·1; N, 8·7. $C_{29}H_{47}O_2N_3$ requires C, 74·4; H, 10·0; N, 8·95%).

The amines listed in the annexed Table were obtained, except where otherwise noted, by catalytic reduction of the corresponding nitro-compounds.

The authors thank Dr. H. J. Barber, F.R.I.C., for his continued interest and helpful discussions, Mr. S. Bance, B.Sc., A.R.I.C., for the semimicro-analyses, and the Directors of May and Baker Ltd. for permission to publish this work.

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DAGENHAM, ESSEX.

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184. *Studies in the Steroid Series. Part LXXII.* The Bromination of 11-Oxo-5β-steroids.*

By E. R. H. Jones and D. J. Wluka.

Bromination of 11-ketones (I) of the 5β-pregnane series gives 12α-bromo-compounds. From the $\Delta^{9(11)}$-enol acetates (II), however, by bromination in the presence of hydrogen bromide acceptors, 9α-bromo-ketones can be prepared; treatment with pyridine converts them into the desired Δ^{8}-11-ketones (V).

In connection with attempts to prepare 9-methylated steroids [1] suitable for conversion either into compounds related to the pentacyclic triterpenes or into analogues of steroid hormones, it was desired to obtain 7 : 8- or 8 : 9-ethylenic 11-ketones of the 5β- or 5α-pregnane (*allo*pregnane) series. Bromination of an 11-ketone belonging to the 5α-steroid series (*i.e.*, 3β-acetoxyergostan-11-one) results in the formation of the 9α-bromo-ketone in good yield,[2] the position of substitution being in accord with the tendency of 11-ketones of this series to enolise towards $C_{(9)}$, *e.g.*, acetylation giving 9 : 11-unsaturated 11-acetates. 11-Ketones of the 5β-series, on the other hand, have been reported to give 12α-bromo-compounds [3] despite the fact that enol acetylation proceeds as in the 5α-series.[4]

(Tertiary bromo)-ketones are converted by hydrogen bromide into the secondary isomers [5] and it has been established that a 9α-bromo-11-ketone in the ergostane series also behaves in this way.[2,6] The isolation [3] of the 12α-bromo-compound of the 5β-pregnane type might well be due to the ready isomerisation of an initial 9-bromo-compound (the yield quoted was only 40%). Of course with the *cis*-AB-junction it is also possible that isomerisation might be facilitated, or bromination prevented, by the greater steric compression on a 9α-bromine atom.

Bromination of 3α : 20β-diacetoxy-5β-pregnan-11-one (Ia) under normal conditions, *i.e.*, at 50° in acetic acid under nitrogen in the dark (cf. ref. 2), gave the 12α-bromo-ketone (IV) in 70% yield. Its structure was proved by its stability to both bases and hydrogen bromide while the absence of any appreciable shift in the infrared carbonyl stretching frequency, and the ultraviolet absorption maximum at *ca.* 3200 Å (Δλ 230 Å), are in agreement with a 12α-configuration.[7] The optical rotatory dispersion † and molecular rotation differences also lead to the same conclusion.

The enol acetate (IIa) was prepared in 80% yield by treatment of the ketone (Ia) with acetic anhydride and toluene-*p*-sulphonic acid. Bromination in acetic acid gave again the 12-bromo-compound (IV), but by adding sodium acetate to the reaction medium or, better, by using pyridine [8] in acetic acid (10%) as solvent, the 9α-bromo-isomer (IIIa) was obtained in high yield. Its structure was proved by (*a*) its light absorption and optical rotatory dispersion,† indicating also axial conformation of the bromine atom, (*b*) its conversion with hydrogen bromide into the isomeric 12α-bromo-ketone (IV), and (*c*) its easy dehydrobromination with boiling pyridine to the Δ^{8}-11-ketone (Va).

An attempt to obtain chemical proof of the configuration of the 9-bromine atom in (IIIa) by the Fieser method [9] was frustrated by the production, on lithium aluminium

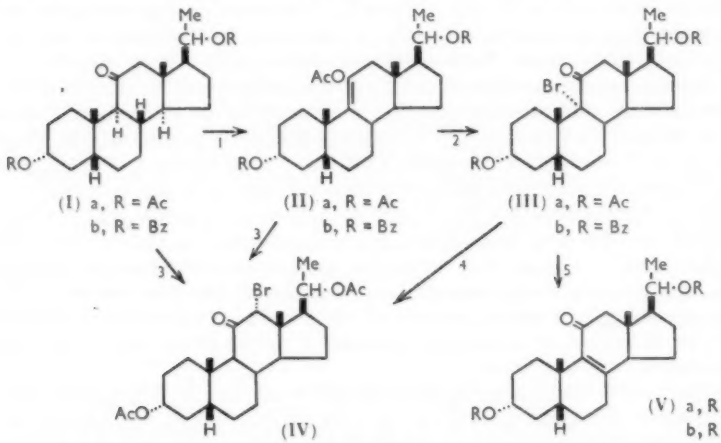
* Part LXXI, *J.*, 1958, 2156.

† We are much indebted to Professor C. Djerassi for these measurements.

[1] Cf. Jones, Meakins, and Stephenson, *J.*, 1958, 2156.
[2] Henbest, Jones, Wagland, and Wrigley, *J.*, 1955, 2477.
[3] Turner, Mattox, Engel, McKenzie, and Kendall, *J. Biol. Chem.*, 1946, **166**, 345; 1948, **173**, 283.
[4] Hirschmann and Wendler, *J. Amer. Chem. Soc.*, 1953, **75**, 2361.
[5] Heilbron, Jones, and Spring, *J.*, 1937, 801.
[6] Wrigley, Ph.D. thesis, Manchester, 1956.
[7] R. N. Jones, Ramsay, Herling, and Dobriner, *J. Amer. Chem. Soc.*, 1952, **74**, 2828; Cookson, *J.*, 1954, 282.
[8] Cf. Corey and Ursprung, *J. Amer. Chem. Soc.*, 1956, **78**, 5041.
[9] Fieser and Ettore, *J. Amer. Chem. Soc.*, 1953, **75**, 1700; Fieser and Dominguez, *ibid.*, p. 1704.

hydride reduction (followed by acetylation), of bromine-free compounds, the ketone (Ia), and the related 11β-alcohol. Sodium borohydride reduction of the related 9α-bromo-ketone in the ergostane series proceeded in a similar manner.[2] With the 12α-bromo-ketone (IV) on the other hand, reduction yielded the expected bromohydrin and this with base gave the 11β : 12β-epoxide.

Although the study so far had been entirely with the diacetate series, it had been realised that it would be preferable to carry out the methylation step on a dibenzoate since *O*-methylation is virtually non-existent with these esters.[10] Under very mild conditions, with dilute methanolic sodium carbonate, it was possible to convert the diacetate into the keto-diol (V; R = H) (characterised by oxidation to 5β-pregn-8-ene-3 : 11 : 20-trione) but this hydrolysis was accompanied by appreciable inversion at $C_{(14)}$.[11] This necessitated



Reagents: 1, Ac_2O–p-$C_6H_4Me{\cdot}SO_3H$. 2, Br–C_5H_5N–AcOH. 3, Br–AcOH. 4, HBr–AcOH. 5, C_5H_5N.

repetition of the (I)—(V) sequence of reactions in the dibenzoate series; results very similar to those already described were obtained. The absence of any significant amount of ester interchange during the preparation of the enol acetate in the dibenzoate series is noteworthy.

Experimental

M. p.s were determined on a Kofler block and are corrected. Rotations were measured for chloroform solutions at room temperature. Infrared spectra, unless otherwise specified, were recorded for carbon disulphide and ultraviolet absorption spectra for ethanol solutions. Usually the alumina used for chromatography was prepared by deactivating Peter Spence's Grade " H " alumina with 5% of 10% acetic acid. Light petroleum refers to the fraction of b. p. 60—80°.

3α : 20β-*Diacetoxy*-12α-*bromo*-5β-*pregnan*-11-*one* (IV).—A solution of 3α : 20β-diacetoxy-pregnan-11-one [12] (1·0 g.) in acetic acid (10 c.c.) was treated in nitrogen in the dark at 50° with a 50% w/v solution (5 drops) of hydrobromic acid in acetic acid, and with bromine (420 mg.; 1·1 mol.) in acetic acid (1·2 c.c.). The flask was then stoppered; after 50 min. the mixture was diluted with ether, and isolation in the normal manner gave the 12α-*bromo-ketone* (860 mg.) as needles (from methanol), m. p. 176—178°, $[\alpha]_D$ −4° (*c* 0·93) (Found: C, 60·3; H, 7·7; Br, 16·1. $C_{25}H_{37}O_5Br$ requires C, 60·3; H, 7·5; Br, 16·1%), $\nu_{max.}$ 1730, 1230 (acetate), 1709 cm.$^{-1}$ (carbonyl), $\lambda_{max.}$ 3190 Å (ε 150). The bromo-ketone was mainly recovered when refluxed in collidine for 7 hr., or in pyridine containing silver nitrate (10%) for 10 hr. No change in rotation

[10] Woodward, Patchett, Barton, Ives, and Kelly, *J.*, 1957, 1131.

[11] Cf. Wendler, Graber, Snoddy, and Bollinger, *J. Amer. Chem. Soc.*, 1957, **79**, 4476. This inversion will be discussed in detail in a later publication.

[12] Sarett, *J. Amer. Chem. Soc.*, 1948, **70**, 1690.

was observed when the bromo-ketone (100 mg.) was kept for 4 days in acetic acid (5 c.c.) containing hydrobromic acid (50% in acetic acid; 15 drops), and the compound was recovered unchanged.

3α : 11 : 20β-*Triacetoxy*-5β-*pregn*-9(11)-*ene* (IIa).—(*a*) A solution of 3α : 20β-diacetoxypregnan-11-one (1·0 g.) in carbon tetrachloride (9·4 c.c.) was treated with acetic anhydride (0·6 c.c.) and 60% aqueous perchloric acid (0·03 c.c.), and kept at 15° for 15 days. The mixture was washed with ice-cold 5% sodium hydroxide solution and water and dried. Evaporation, and repeated recrystallisation of the product from acetone–light petroleum, gave needles of the *enol acetate* (400 mg.), m. p. 224—228°, $[\alpha]_D$ +90° (*c*, 1·02) (Found: C, 70·4; H, 8·65. $C_{27}H_{40}O_6$ requires C, 70·4; H, 8·75%), $\nu_{max.}$ 1733, 1235 (acetate), 1640 (C=C stretching), and 1752 (sh) and 1212 cm.$^{-1}$ (11-acetate).

(*b*) The solvent was fractionally distilled from a solution of 3α-acetoxy-20β-hydroxy-5β-pregnan-11-one (23·3 g.) and toluene-*p*-sulphonic acid (8 g.) in acetic anhydride (600 c.c.; acetic acid-free), while acetic anhydride was added periodically to keep the volume approximately constant. After 10 hr., the residual solvent was removed under reduced pressure, and methanol was added cautiously to the cooled residue. A small volume of water was added, followed by solid potassium hydrogen carbonate; the product was then isolated *via* ethyl acetate. After two recrystallisations from acetone, the enol acetate (20·3 g., 78%) was obtained as needles, m. p. 224—228°, identical with the above product.

3α : 20β-*Diacetoxy*-9α-*bromo*-5β-*pregnan*-11-*one* (IIIa).—(*a*) Bromine (5·9 g., 1·5 mol.) in acetic acid (18 c.c.) was added to a solution of the above enol acetate (11·3 g.) in 10% v/v pyridine–acetic acid (400 c.c.) in nitrogen. The flask was stoppered, and stored at 30° for 30 hr. in the dark. Sodium sulphite was added and the product was isolated in the usual manner with ether, being dried by azeotropic distillation with benzene under reduced pressure. The 9α-*bromo-ketone* separated from methanol as an amorphous solid (9·5 g.), with m. p. 152—154° when the sample was placed on the block at 140° and heated rapidly. It decomposes fairly rapidly at 100° and slowly at 20°, even in the dark. The bromo-ketone was also readily characterised by its rotation, $[\alpha]_D$ +170° (*c* 1·04), which differed appreciably from those of the enol acetate, 11-ketone, or the 12α-bromo-ketone (Found: C, 60·4; H, 7·45; Br, 15·5. $C_{25}H_{37}O_5Br$ requires C, 60·3; H, 7·5; Br, 16·1%). It had infrared peaks at 1730, 1230 (acetate), and 1709 cm.$^{-1}$ (11-ketone), and ultraviolet absorption max. 3200 Å (ε 100).

(*b*) When the enol acetate (500 mg.) in acetic acid (20 c.c.) containing fused sodium acetate (500 mg.) was treated with bromine (0·21 g., 1·2 mol.) for 24 hr. at 30° in the dark, the 9α-bromo-ketone was obtained in 45% yield. In the absence of sodium acetate, the 12α-bromo-isomer was isolated in 70% yield.

Isomerisation of the **9α-** *into the* **12α-*Bromo-ketone*** (IIIa ⟶ IV).—A solution of 3α : 20β-diacetoxy-9α-bromo-5β-pregnan-11-one (40 mg.) in acetic acid (8 c.c.) containing hydrobromic acid (50% in acetic acid; 3 drops) was kept at 15° for 2½ days, during which the rotation of the solution changed from +0·8° to +0·1°. (The 12α-bromo-ketone has an appreciable positive rotation in acetic acid, as compared with $[\alpha]_D$ −4° in chloroform.) Isolation *via* ether, and crystallisation from methanol, gave the 12α-bromo-ketone (17 mg.), m. p. and mixed m. p. 175—178°.

3α : 20β-*Diacetoxy*-5β-*pregn*-8-*en*-11-*one* (Va).—A solution of the 9α-bromo-ketone (2·52 g.) and silver nitrate (8·7 g.) in pyridine (70 c.c.) was heated under reflux for 2½ hr. (but see below). The product obtained *via* ether was dissolved in benzene and filtered through alumina (100 g.). Evaporation and crystallisation of the residue from acetone–methanol gave needles of the αβ-unsaturated *ketone* (1·15 g.), m. p. 76°, and 162—166° after resolidification. Crystallisation from acetone–light petroleum gave needles, m. p. 166—167°, $[\alpha]_D$ +128° (*c* 1·13) (Found: C, 71·9; H, 8·55. $C_{25}H_{36}O_5$ requires C, 72·1; H, 8·7%), $\nu_{max.}$ (in Nujol) 1724, 1250 (acetate), 1650 (αβ-unsaturated ketone), 1595 (8-ene) and 1072 cm.$^{-1}$, $\lambda_{max.}$ 2540 Å (ε 8000).

In a subsequent experiment, in which the bromo-ketone was not isolated and dehydrobromination was effected by refluxing in pyridine alone for 15 min., the enol acetate (IIa) (20·6 g.) gave 14·8 g. of conjugated ketone (Va).

3α : 20β-*Dihydroxy*-5β-*pregn*-8-*en*-11-*one* (V; R = H).—3α : 20β-Diacetoxy-5β-pregn-8-en-11-one (240 mg.) in methanol (40 c.c.) was treated with potassium carbonate (400 mg.) in water (4 c.c.), and kept for 3 days at 17°. The solution was neutralised with acetic acid, then concentrated under diminished pressure, and ether and chloroform were added. The recovered steroid was adsorbed on alumina (10 g.); benzene–ether (1 : 1) eluted partially saponified

material (105 mg.), and acetone then eluted the conjugated *keto-diol* (V; R = H; 105 mg.), which crystallised from acetone in needles, m. p. 213—219°, $[\alpha]_D$ +128° (*c* 0·76) (Found: C, 75·5; H, 9·5. $C_{21}H_{32}O_3$ requires C, 75·8; H, 9·7%), $\nu_{max.}$ (in Nujol) 3200—3300 (hydroxyl), 1654 (αβ-unsaturated ketone), and 1593 cm.$^{-1}$ (8-ene), $\lambda_{max.}$ 2540 Å (ε 8000).

The keto-diol (20 mg.), treated overnight at 20° with acetic anhydride (0·5 c.c.) and pyridine (0·5 c.c.), gave back the parent diacetate (20 mg.), m. p. (and mixed) 163—165°, $[\alpha]_D$ +128° (*c* 1·04).

5β-*Pregn*-8-*ene*-3 : 11 : 20-*trione*.—3α : 20β-Dihydroxy-5β-pregn-8-en-11-one (130 mg.) in acetone was oxidised with 8N-chromic acid.[13] The product was recovered *via* ether and recrystallised from methanol, to give the *trione* as needles, m. p. 195—199°, $[\alpha]_D$ +152° (*c* 1·0) (Found: C, 76·5; H, 8·85. $C_{21}H_{28}O_3$ requires C, 76·8; H, 8·6%), $\lambda_{max.}$ 2530 Å (ε 8000), $\nu_{max.}$ (in Nujol) 1709 (3 : 20-dione), 1650 (αβ-unsaturated ketone), and 1598 cm.$^{-1}$ (8 : 9-ene).

3α : 20β-*Dibenzoyloxy*-5β-*pregnan*-11-*one* (Ib).—3α : 20β-Dihydroxy-5β-pregnan-11-one [13] was treated with pyridine–benzoyl chloride in the usual way. The *dibenzoate* crystallised from ethyl acetate in thick prisms, m. p. 217—219°, $[\alpha]_D$ +47° (*c* 1·07) (Found: C, 77·8; H, 7·85. $C_{35}H_{42}O_5$ requires C, 77·5; H, 7·85%), $\nu_{max.}$ 1720 (benzoate and 11-ketone, not resolved) and 1270 cm.$^{-1}$ (benzoate).

11-*Acetoxy*-3α : 20β-*dibenzoyloxy*-5β-*pregn*-9(11)-*ene* (IIb).—The solvent was fractionally distilled from a solution of the keto-dibenzoate (64·9 g.) and toluene-*p*-sulphonic acid (20 g., *ca.* 1 mol.) in acetic anhydride (1·2 l.; acetic acid-free). After 4 hr., further acetic anhydride (400 c.c.) was added slowly, and after 9 hr., when the volume of the reaction mixture had been reduced to *ca.* 500 c.c., heating was discontinued. The solid which separated overnight was filtered off, washed liberally with ether, and finally with methanol, giving the *enol acetate* (59·4 g.) as needles, m. p. 236—242°. A sample recrystallised from ethyl acetate had m. p. 240—242°, $[\alpha]_D$ +56° (*c* 1·01) (Found: C, 75·9; H, 7·4. $C_{37}H_{44}O_6$ requires C, 76·0; H, 7·6%), $\nu_{max.}$ 1761, 1270 (11-acetate), 1720, 1270 (benzoate), and 1650 cm.$^{-1}$ (9 : 11-ene).

3α : 20β-*Dibenzoyloxy*-9α-*bromo*-5β-*pregnan*-11-*one* * (IIIb).—A solution of the above enol acetate dibenzoate (39·4 g.) in dry chloroform (100 c.c.) was diluted with glacial acetic acid (1 l.) and pyridine (100 c.c.). Nitrogen was bubbled into the flask for 5 min., and bromine (16·2 g.; 1·5 mol.) in acetic acid (70 c.c.) was added. The flask was stoppered, and kept at 30° in the dark for 26 hr., with periodical shaking to facilitate reaction of undissolved material. Sodium sulphite was added, and the product was isolated *via* ether. The 9α-*bromo-ketone* (32·1 g.) separated from ethyl acetate as prisms, m. p. 169—170° (sample placed on block at 160°), $[\alpha]_D$ +122° (*c*, 1·15) (Found: C, 67·7; H, 6·5; Br, 13·2. $C_{35}H_{41}O_5Br$ requires C, 67·6; H, 6·65; Br, 12·9%), $\nu_{max.}$ 1720, 1271 cm.$^{-1}$ (benzoate).

3α : 20β-*Dibenzoyloxy*-5β-*pregn*-8-*en*-11-*one* (Vb).—A solution of the 9α-bromo-ketone (5 g.) in pyridine (60 c.c.) was heated under reflux for 8 min. A large volume of ether was added, and the resulting solution was washed repeatedly with dilute hydrochloric acid. The product was then recovered in the usual manner, and recrystallised from methanol to give the conjugated *ketone* (2·9 g.) as prisms, m. p. 152—154°, $[\alpha]_D$ +18° (*c* 1·38). The compound was also obtained as needles, m. p. 132—134°, the two forms being interconvertible in solution (Found: C, 77·6; H, 7·45. $C_{35}H_{40}O_4$ requires C, 77·7; H, 7·45%); it had infrared peaks at 1719, 1265 (benzoate), and 1658 cm.$^{-1}$ (αβ-unsaturated ketone).

Lithium Aluminium Hydride Reduction of the 12α-*Bromo-ketone*.—A solution of the 12α-bromo-ketone (0·50 g.) in dry ether (25 c.c.) and lithium aluminium hydride (53 mg., 1·38 mol.) were heated under reflux for 1 hr. The steroid was isolated *via* ether, acetylated, and then chromatographed on alumina (45 g.). Benzene–light petroleum (2 : 1) eluted starting material (120 mg.); benzene–ether (10 : 1) eluted 3α : 20β-*diacetoxy*-12α-*bromo*-5β-*pregnan*-11β-*ol* (270 mg.), which crystallised from methanol as plates, m. p. 204—207°, $[\alpha]_D$ +91° (*c* 1·03) (Found: C, 60·1; H, 8·0; Br, 16·4. $C_{25}H_{39}O_5Br$ requires C, 60·1; H, 7·9; Br, 16·0%), $\nu_{max.}$ (in Nujol) 3500 (hydroxyl), 1733 and 1235 cm.$^{-1}$ (acetate).

3α : 20β-*Diacetoxy*-11β : 12β-*epoxy*-5β-*pregnane*.—A solution of the bromohydrin (130 mg.) in *tert.*-butyl alcohol (10 c.c.) was treated with M-potassium *tert.*-butoxide (2 c.c.) in *tert.*-butyl alcohol. The solution was kept at 55° for 15 min.; the steroid was recovered *via* ether and reacetylated at room temperature. The product in benzene was passed down a column of

* This experiment was carried out by Dr. J. S. G. Cox.

[13] Bowers, Halsall, Jones, and Lemin, *J.*, 1953, 2548.

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alumina (5 g.), then crystallised from methanol to give the 11β : 12β-*epoxide* as plates, m. p. 159—160°, $[\alpha]_D$ +74° (*c* 1·14) (Found: C, 71·8; H, 8·8. $C_{25}H_{38}O_5$ requires C, 71·75; H, 9·1%), $\nu_{max.}$ 1737 and 1237 cm.$^{-1}$ (acetate), but no hydroxyl band.

Lithium Aluminium Hydride Reduction of the 9α-*Bromo-ketone* (IIIa).—A solution of the ketone (IIIa) (620 mg.) in anhydrous ether (30 c.c.) was heated under reflux for 1 hr. with lithium aluminium hydride (66 mg., 1·38 mol.). The steroid was isolated *via* ether, acetylated, and chromatographed on alumina (55 g.). Benzene–light petroleum (2 : 1) eluted starting material (50 mg.); further elution with the same solvent and with benzene gave the parent 11-keto-diacetate (215 mg.), needles (from methanol), m. p. (and mixed) 160—161°; finally benzene–ether (10 : 1) eluted 3α : 20β-*diacetoxy*-5β-*pregnan*-11β-*ol* (230 mg.), plates (from methanol), m. p. 171—172°, $[\alpha]_D$ +69° (*c* 1·25), $[\alpha]_D$ +89° (*c* 1·07; in acetone) (Found: C, 71·4; H, 9·35. $C_{25}H_{40}O_5$ requires C, 71·4; H, 9·6%). This 11β-hydroxy-compound was identical with that obtained by reduction of the 11-keto-diacetate with sodium borohydride by the method of Oliveto and Hershberg.[14] It had infrared peaks (in Nujol) at 3500 (hydroxyl), 1737 and 1235 cm.$^{-1}$ (acetate).

The authors are indebted to Merck and Co., Rahway, N.J., for gifts of starting material and to the University of Queensland for a Research Scholarship (to D. J. W.).

THE DYSON PERRINS LABORATORY, OXFORD UNIVERSITY. [*Received, October 23rd*, 1958.]

[14] Oliveto and Hershberg, *J. Amer. Chem. Soc.*, 1953, **75**, 488. Dr. Hershberg has very kindly informed us that the constants originally quoted for 3α : 20β-diacetoxy-5β-pregnan-11β-ol (m. p. 119—120°, $[\alpha]_D$ +68° in acetone) have not been confirmed on repetition of the preparation. He now finds m. p. 165—170°, $[\alpha]_D$ +69° (in dioxan), similar to the values indicated above.

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185. *Studies in the Steroid Series. Part LXXIII.* The Bromination of 7-Oxo-steroids.*

By E. R. H. JONES and D. J. WLUKA.

Treatment of 7-oxo-5α-cholestanyl acetate (II) with acetic anhydride–toluene-*p*-sulphonic acid gives a mixture of the Δ^6- and Δ^7-eno lacetates (I and III), separable by chromatography. Bromination of these under normal conditions leads to 6-bromo-compounds (IV and V), but in the presence of bases bromination of the ketone (II) gives the hitherto unknown 8β-bromo-compound (VI).

THE acid-catalysed bromination of 7-oxo-5α-cholestanyl acetate (II) yields the 6β-bromo-compound (V), transformed in the presence of hydrogen bromide into the more stable 6α(equatorial)-isomer (IV).[1,2] Further bromination of either isomer yields a 6 : 6-dibromo-compound. From these observations and other data it has been concluded [3] that enolisation of this 7-keto-steroid takes place to give the Δ^6-rather than the Δ^7-enol and suggested that the shielding of the 8β-hydrogen atom by the angular methyl groups is partly responsible. A possible explanation of the isolation of only 6-substituted bromination products is that enolisation towards the 8-position does occur, but that any 8-bromo-compound initially formed is very rapidly isomerised under the experimental conditions employed, *i.e.*, in the presence of hydrogen bromide. This view received some support from the behaviour of the 9-bromo-11-keto-compounds described in the preceding paper,[4] and some experiments with 7-keto-compounds were therefore initiated.

In this case, however, preparative indications were much less favourable and we could

* Part LXXII, preceding paper.

[1] Barr, Heilbron, Jones, and Spring, *J.*, 1938, 334.
[2] Configurations suggested by Fieser and Fieser, "Natural Products related to Phenanthrene," 1948, p. 270, and confirmed by Cookson, *J.*, 1954, 282.
[3] Corey and Sneen, *J. Amer. Chem. Soc.*, 1956, **78**, 6269.
[4] Cf. Wrigley, Ph.D. thesis, Manchester, 1956.

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find no example of the production of a Δ^7-enol acetate. Hirschmann, Brown, and Wendler [5] treated methyl 3α-acetoxy-7 : 12-dioxocholanate with acetic anhydride and toluene-*p*-sulphonic acid, obtaining a 44% yield of a crystalline enol acetate, later [6] proved to be the Δ^6-isomer by oxidative degradation. There was a substantial amount of non-crystalline product from this experiment; this gave a moderate yield of the parent ketone on hydrolysis and, assuming that it was the Δ^7-isomer, we carried out similar experiments with 7-oxocholestanyl acetate.

In acetic anhydride containing toluene-*p*-sulphonic acid the ketone (II) was converted to the extent of 60% into a mixture of the Δ^6- and Δ^7-enol acetates (I and III), separated from one another and from starting material by chromatography. Although neither (I) nor (III) crystallised (not uncommon with steroid enol acetates), they were easily differentiated by their optical rotations (−55° and −10° respectively), by their behaviour on bromination (see below), and by their infrared spectra. The spectra differed most markedly in the range 1050—1180 cm.$^{-1}$ and that of the Δ^6-isomer (I) contained a pair of weak bands at 800 and 820 cm.$^{-1}$ which were assigned to the C–H of the 6 : 7-double bond. The signs of the optical rotations of (I) and (II) are in agreement with the values for Δ^6-cholestenes [7] and Δ^7-cholestenes.[8]

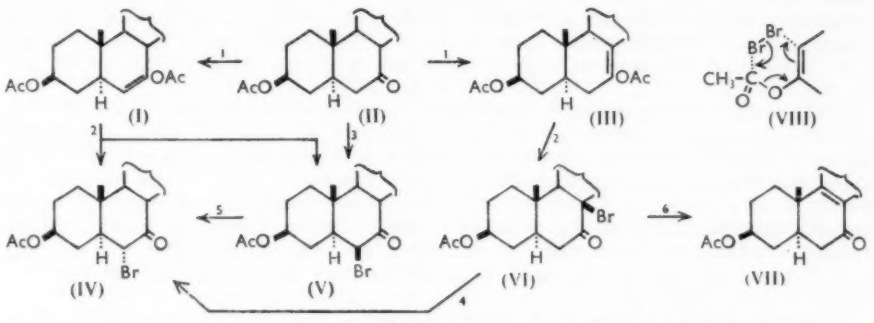
In *iso*propenyl acetate containing toluene-*p*-sulphonic acid, the Δ^6-isomer was formed in 25% yield, none of the other isomer could be detected, and most of the unconverted ketone (II) was recovered. Neither of the isomers was observed to rearrange under these conditions. A detailed study of the relative stabilities of the isomers (I) and (III) under the conditions used in their preparation was not possible because of substantial losses of material (usually *ca.* 30% of the starting material could not be eluted from deactivated alumina and this amount increased with increasing concentration of the acid catalyst). The relative yields of the two isomers (I and III) varied usually in the range 1·2—2 : 1, although in one experiment in which acetic acid was rigorously removed before addition of the ketone the ratio reached 6·5 : 1. None of the Δ^7-isomer (III) could be detected in an attempted isomerisation of (I), and only a 20% conversion (based on total recovered enol acetates) of (III) into (I) was achieved. It was concluded that both enol acetates are formed, simultaneously, in acetic anhydride and that the Δ^7-isomer is gradually converted into the more stable Δ^6-isomer.

Bromination of the Δ^6-enol acetate (I), in pyridine–acetic acid, gave a mixture (separated by chromatography) of the two monobromo-compounds (IV and V) (75% yield) together with some 7-oxocholesteryl acetate. Control experiments showed that the bromo-compounds were unaffected on alumina and, apart from partial dehydrobromination, the 6β-isomer (V) was recovered unchanged after prolonged treatment under the bromination conditions (*i.e.*, by bromine and pyridine hydrobromide in pyridine–acetic acid). Whereas direct bromination of the ketone (II) with bromine in chloroform gives *ca.* 55% of the 6β(axial)-isomer (V), a stereoelectronic factor counteracting the steric factor favouring equatorial attack of the reagent,[3] in this case the product of equatorial attack (*i.e.*, IV) predominates to the extent of 5 : 1, or 2·5 : 1 if it is assumed that the whole of the unsaturated ketone is derived from the axial isomer. It seems improbable that stereoelectronic control such as is involved in the acid-catalysed enolisation process is operative here. A cyclic transition state such as (VIII) could be operative in enol acetate brominations; this would appear to favour equatorial introduction of the 6-bromine atom.

Bromination of the Δ^7-isomer (III) in the presence of pyridine gave, in 45% yield, the new 8β-bromo-ketone (VI). Dehydrobromination with pyridine yielded 3β-acetoxy-5α-cholest-8-en-7-one (VII) with constants identical with those of Fieser [9] except in extinction

[5] Hirschmann, Brown, and Wendler, *J. Amer. Chem. Soc.*, 1951, **73**, 5373.
[6] Hirschmann and Wendler, *ibid.*, 1953, **75**, 2361.
[7] James, Rees, and Shoppee, *J.*, 1955, 1370.
[8] Barton, *J.*, 1945, 813.
[9] Fieser, *J. Amer. Chem. Soc.*, 1953, **75**, 4395.

coefficient (ε 10,100, compared with 15,500). The values found [10,11] for a number of compounds with the same chromophoric system in the ergosterol series do not exceed 10,000.



Reagents: 1, Ac_2O–*p*-$C_6H_4Me{\cdot}SO_3H$. 2, Br–C_5H_5N–AcOH. 3, Br–$CHCl_3$. 4, HBr–$CHCl_3$–AcOH. 5, HBr–AcOH. 6, C_5H_5N.

The effect of hydrogen bromide on the 8β-bromo-ketone (VI) was highly dependent upon the solvent. In dry chloroform this compound was recovered unchanged, in chloroform–acetic acid (1 : 1) the 6α-bromo-ketone (IV) (60%) and debrominated ketone (II) (35%) resulted, whilst in acetic acid the ratio (IV) : (II) was *ca.* 1 : 3, debromination predominating. It appears that in acetic acid alone, rebromination does not occur, in line with the original observation [1] that the ketone (II) is not brominated at an appreciable rate in acetic acid at room temperature. The absence of isomerisation in the chloroform experiment suggests that in the direct bromination experiments (although the conditions were not strictly comparable), little or no bromination occurs at position 8. It is hoped that more direct information will be forthcoming from a study of the bromination of 3β-acetoxy-8β-deuterocholestan-7-one which should now be accessible *via* (VI) by debromination with zinc and deuteroacetic acid (AcOD).

Infrared and ultraviolet absorption spectra established the axial nature of the 8-bromine atom in (VI), and complete proof of its 8β-configuration was provided by comparison of its optical rotatory dispersion curve with those of the parent ketone (II) and the isomeric 6-bromo-compounds (IV and V). As was expected the β(axial)-compounds (V and VI) showed large Cotton effects and bathochromic shifts as compared with those of the unsubstituted ketone and the 6α(equatorial)-bromo-compound (VI).[12] It was not possible to obtain chemical proof of the 8β-configuration of the bromine atom since reduction of the bromo-ketone (VI) with lithium aluminium hydride gave the parent ketone (II) together with material readily converted on treatment with base into compounds containing conjugated diene chromophores.

Experimental

General directions are given in the preceding paper.

Enol-acetylation of 7-Oxo-5α-cholestanyl Acetate (II).—(*a*) The solvent was fractionally distilled through a short column packed with glass helices from a solution of the ketone (6·6 g.) and toluene-*p*-sulphonic acid (2·85 g.) in acetic anhydride (150 c.c.), more anhydride being added periodically to keep the volume approximately constant. After 9 hr. the solvent was evaporated under reduced pressure, methanol was added to the brown gum to decompose any remaining anhydride, and the steroid was recovered in the usual manner. The product was chromatographed on alumina (600 g.); benzene–light petroleum (1 : 2; 4 × 300 c.c.) eluted 3β : 7-*diacetoxy*-5α-*cholest*-6-*ene* (I) (1·99 g.); further elution with the same solvent mixture

[10] Elks, Evans, Long, and Thomas, *J.*, 1954, 451.
[11] Budziarek, Newbold, Stevenson, and Spring, *J.*, 1952, 2892.
[12] Djerassi, Osiecki, Riniker, and Riniker, *J. Amer. Chem. Soc.*, 1958, **80**, 1216.

(7 × 300 c.c.) yielded 3β : 7-*diacetoxy-5α-cholest-7-ene* (III) (1·75 g.); finally, benzene eluted starting material (1·31 g.). Neither enol acetate crystallised. The Δ^6-enol acetate (I) had $[\alpha]_D$ −55° (*c* 0·97) (Found: C, 76·6; H, 10·4. $C_{31}H_{50}O_4$ requires C, 76·5; H, 10·4%), $\nu_{max.}$ 1736, 1235 (3-acetate), 1754 (sh), 1215 (7-acetate), and 1675, 800, and 820 cm.$^{-1}$ (6-ene). The Δ^7-enol acetate (III) had $[\alpha]_D$ −10° (*c* 1·13) (Found: C, 76·5; H, 10·2%), $\nu_{max.}$ 1736, 1236 (3-acetate), 1754 (sh), 1217 (7-acetate), and 1673 cm.$^{-1}$ (7-ene). The infrared spectra of the two isomers were very similar, but they could be distinguished by differences in the 1050—1180 cm.$^{-1}$ region.

(*b*) The solvent was fractionally distilled from a solution of 7-oxocholestanyl acetate (3·3 g.) and toluene-*p*-sulphonic acid (0·5 g.) in *iso*propenyl acetate (60 c.c.); the volume of the solution was maintained at *ca.* 50 c.c. by periodic addition of *iso*propenyl acetate. After 7 hr. the solvent was removed under reduced pressure and the steroid recovered in the usual manner. Starting material (1·4 g.), m. p. 151—153°, crystallised from a solution of the product in acetone–methanol, and the material (1·53 g.) from the mother-liquors was chromatographed on alumina (120 g.). Benzene–light petroleum (1 : 3) eluted 3β : 7-diacetoxycholest-6-ene (750 mg.; $[\alpha]_D$ −55°); benzene–light petroleum (1 : 1) then eluted more starting material (600 mg.), m. p. and mixed m. p. 150—152°.

Isomerisation of the Δ^7*-Enol Acetate* (III).—A solution of the Δ^7-enol acetate (910 mg.) and toluene-*p*-sulphonic acid (70 mg.; 0·2 mol.) in acetic anhydride (60 c.c.; acetic acid-free) was fractionally distilled, 20 c.c. of distillate being collected during 2 hr. After a further 1½ hours' heating under reflux, the acetic anhydride was removed under reduced pressure and the product, recovered *via* ether, was adsorbed on alumina (90 g.). Benzene–light petroleum (1 : 3; 100 c.c.) eluted 75% pure 3β : 7-diacetoxycholest-6-ene (140 mg.; identified by its infrared absorption and $[\alpha]_D$ −42°), and further elution with the same solvent mixture (350 c.c.) afforded starting material (540 mg.; identified by its infrared absorption and $[\alpha]_D$ −10°). Finally, benzene (100 c.c.) eluted 3α-acetoxycholestan-7-one (50 mg.), plates (from acetone–methanol), m. p. and mixed m. p. 151—153°.

Attempted Isomerisation of the Δ^6*-Enol Acetate* (I).—Acetic anhydride (150 c.c.) containing toluene-*p*-sulphonic acid (180 mg.) was fractionally distilled until the still-head temperature ceased to rise. After the Δ^6-enol acetate (2·0 g.) in acetic anhydride (20 c.c.; acetic acid-free) had been added, the solution was concentrated to *ca.* 100 c.c., and then heated under reflux for 3 hr. After isolation as above, the product was adsorbed on alumina (200 g.). Benzene–light petroleum (1 : 4) eluted starting material (0·99 g.; identified by its infrared absorption), but none of the Δ^7-enol acetate could be detected. Elution with benzene–light petroleum (1 : 1) and then with benzene afforded ketonic material (300 mg.), shown by its infrared absorption to be impure 3β-acetoxycholestan-7-one.

Bromination of 3β : 7-*Diacetoxy-5α-cholest-6-ene* (I).—Bromine (220 mg., 1·5 mol.) in acetic acid (0·6 c.c.) was added to a solution of the above enol acetate (450 mg.) in 1 : 10 v/v pyridine–acetic acid (5·5 c.c.) under nitrogen. The flask was stoppered and kept in the dark at 20° for 25 hr. An aqueous solution of sodium sulphite was then added, and the product isolated *via* ether and adsorbed on alumina (50 g.). Benzene–light petroleum (1 : 2) eluted in succession 6β-bromo-7-oxocholestanyl acetate (V) (64 mg.), needles (from acetone–methanol), m. p. and mixed m. p. 172—174°, and 6α-bromo-7-oxocholestanyl acetate (IV) (310 mg.), needles (from aqueous acetic acid), m. p. and mixed m. p. 147—148°; finally, benzene eluted 7-oxocholest-5-enyl acetate (53 mg.), prisms (from acetone–methanol), m. p. and mixed m. p. 160—162°.

Bromination of 3β : 7-*Diacetoxy-5α-cholest-7-ene* (III).—Bromine (910 mg., 1·5 mol.) in acetic acid (2·5 c.c.) was added to a solution of the above enol acetate (1·85 g.) in 1 : 10 v/v pyridine–acetic acid (22 c.c.) in nitrogen. The flask was stoppered, and stored at 17° for 24 hr. in the dark. Sodium sulphite was added, and the steroid was recovered *via* ether. The product was adsorbed on a column of alumina (200 g.); benzene–light petroleum (2 : 5) eluted 8β-*bromo-7-oxo-5α-cholestanyl acetate* (VI) (900 mg.), needles (from ethyl acetate–methanol), m. p. 135—137° (decomp.; the sample being placed on the block 10° below the m. p.), $[\alpha]_D$ −113° (*c* 1·06) (Found: C, 66·7; H, 9·0; Br, 15·6. $C_{29}H_{47}O_3Br$ requires C, 66·5; H, 9·1; Br, 15·3%), $\nu_{max.}$ 1739, 1238 (acetate), and 1718 cm.$^{-1}$ (7-ketone), $\lambda_{max.}$ 3050 Å (ε 106) [ketone (II) has max. at 2830 Å (ε 40)]. Further elution with benzene yielded conjugated ketonic material, plates (from methanol), m. p. 148—154°, $\lambda_{max.}$ 2540 Å (ε 10,000) (see below).

7-*Oxocholest-8-enyl Acetate* (VII).—A solution of the 8β-bromo-ketone (85 mg.) in pyridine (1 c.c.) was kept overnight at 30° and then at 100° for 1 hr. After the pyridine had been

removed under reduced pressure the residue was dissolved in ether and washed several times with dilute hydrochloric acid, water, and finally aqueous sodium hydrogen carbonate. The recovered steroid (67 mg.) was adsorbed on alumina (7 g.) and eluted with benzene–light petroleum (1 : 1; 7 × 5 c.c.), and then with benzene–light petroleum (5 : 1; 10 c.c.). Each fraction showed an absorption maximum at 2525 Å, the extinction coefficient being greatest (10,000) in the last four fractions. These (35 mg.) on crystallisation from methanol gave the conjugated ketone as needles, m. p. 154—157°, $[\alpha]_D$ −34° (*c* 0·87), $\lambda_{max.}$ 2525 Å (ε 10,100). Fieser [8] gives m. p. 155—156°, $[\alpha]_D$ −32·3°, $\lambda_{max.}$ 2530 Å (ε 15,500).*

Treatment of the 8β-*Bromo-ketone* (VI) *with Hydrogen Bromide.*—(a) *In chloroform.* The rotation of a solution of the 8β-bromo-ketone (45 mg.) in dry chloroform (7 c.c.) containing hydrogen bromide (0·1 c.c.; 50% in acetic acid) did not change during 3 hr. After 7 hr., the steroid was recovered *via* ether; crystallisation from ethyl acetate–methanol gave starting material (30 mg.), m. p. and mixed m. p. 135—137° (decomp.).

(b) *In chloroform–acetic acid.* The rotation (1 dm. tube) of a solution of the 8β-bromo-ketone (140 mg.) in chloroform–acetic acid (1 : 1; 15 c.c.) containing hydrogen bromide (0·4 c.c.; 50% in acetic acid) changed from −0·80° to −0·32° in 7½ hr.; the solution had then become too dark for further observations to be made. After 10 hr., the steroid was isolated *via* ether and adsorbed on alumina (15 g.); benzene–light petroleum (1 : 2) eluted starting material (52 mg.), m. p. and mixed m. p. 134—137° (decomp.) after two recrystallisations from ethyl acetate–methanol, and 6α-bromo-7-oxo-5α-cholestanyl acetate (53 mg.), which after recrystallisation from acetone–methanol and from aqueous acetic acid had m. p. and mixed m. p. 142—146°; further elution with benzene–light petroleum (4 : 1) gave 7-oxo-5α-cholestanyl acetate (30 mg.), plates (from acetone–methanol), m. p. and mixed m. p. 151—153°.

(c) *In acetic acid.* The rotation (1 dm. tube) of a solution of the 8β-bromo-ketone (200 mg.) in acetic acid (7 c.c.) containing hydrogen bromide (0·2 c.c.; 50% in acetic acid) changed from −2·78° to −2·25° in 70 min. After 7½ hr. the product was isolated *via* ether and chromatographed on alumina (25 g.), elution being effected with benzene–light petroleum (1 : 2; 7 × 15 c.c.), and benzene–light petroleum (2 : 1; 5 × 15 c.c.). Fractions 4—12 (incl.) consisted of 7-oxo-5α-cholestanyl acetate (110 mg.), m. p. and mixed m. p. 151—153°; the first three fractions (40 mg.) contained principally 6α-bromo-7-oxo-5α-cholestanyl acetate, as shown by their infrared spectra, but a pure sample could not be obtained by crystallisation.

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THE DYSON PERRINS LABORATORY, OXFORD UNIVERSITY. [*Received, October 23rd,* 1958.]

* Unfortunately the only sample which Professor Fieser had retained, and which he kindly sent to us, had deteriorated on storage so that further elucidation of the intensity discrepancy was not possible.

186. *The Synthesis of Polycyclic Aromatic Compounds. Part II.*[1] *Picene-5 : 6- and -13 : 14-quinone and Picene-5 : 6 : 7 : 8-diquinone.*

By W. DAVIES and B. C. ENNIS.

A new application of the Diels–Alder reaction is the use of *o*-quinones with vinylarenes. 1-Vinylnaphthalene and 3-bromo-1 : 2-naphthaquinone form picene-5 : 6-quinone (III) which, together with a smaller amount of picene-13 : 14-quinone, is now separated from the "picene quinone" described in the literature. Oxidation of the monoquinone (III) gives picene 5 : 6 : 7 : 8-diquinone.

THE synthesis of polycyclic quinones, and thence of their parent aromatic hydrocarbons, by the Diels–Alder reaction of *p*-quinones with 1-vinylnaphthalene and related dienes (Part I [1]) suggests a similar synthetic rôle for *o*-quinones. Though some substituted *o*-benzoquinones will react with active dienes, their instability often leads to low yields (and more than one adduct).[2] However, the use of relatively stable *o*-quinones was more hopeful

[1] Part I, Davies and Porter, *J.*, 1957, 4967.

[2] Smith and Hac, *J. Amer. Chem. Soc.*, 1936, **58**, 229; Horner and Merz, *Annalen*, 1950, **570**, 89; Horner and Spietschka, *ibid.*, 1953, **579**, 159; Barltrop and Jeffreys, *J.*, 1954, 154.

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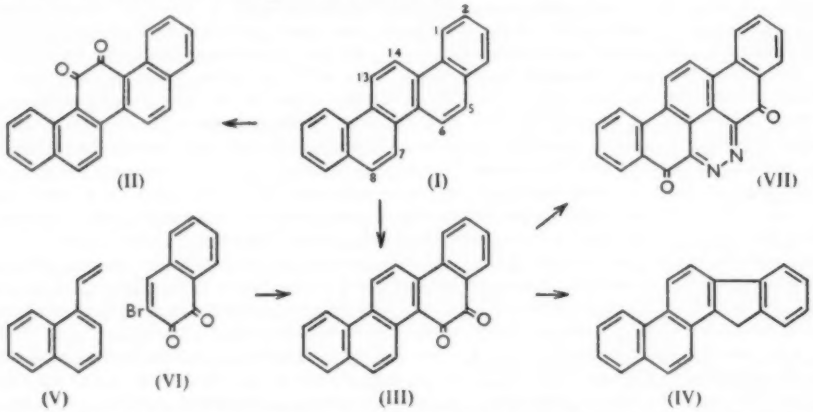
as satisfactory yields had been reported [3] from 2 : 3-dimethylbutadiene and 1 : 2- and 3 : 4-phenanthraquinone and substituted 1 : 2-naphthaquinones.

" Picenequinone," of obscure structure, was obtained by Bamberger and Chattaway [4] by oxidation of picene (I) with chromic acid; it was degraded through a ketone and an acid to 2 : 2′-dinaphthyl, and so was assigned structure (II). On the other hand, Cook,[5] using the original specimen of ketone prepared [4] by heating " picenequinone " with litharge, found it to be a complex mixture from which he chromatographically isolated naphtho(2′ : 1′-1 : 2)fluorenone, which was reduced with hydrazine hydrate to naphtho(2′ : 1′-1 : 2)-fluorene (IV). Cook accordingly accepted the structure of " picenequinone " as essentially (III), and attributed the isolation of 2 : 2′-dinaphthyl " to the presence of impurity in the ' picenic acid ' used by Bamberger and Chattaway."



1-Vinylnaphthalene (V) reacts with 1 : 2 naphthaquinone in acetic acid to form a tar, but with 3-bromo-1 : 2-naphthaquinone (VI) gives >30% of picene-5 : 6-quinone (III), m. p. 310°, which is the only new product isolated. Excess of quinone was used and the initial product was formed, dehydrobrominated, and dehydrogenated in the one operation, as in the self-condensation of 3-bromothionaphthen 1 : 1-dioxide.[6] The compound of m. p. 310° might theoretically be an unknown quinone of 5 : 6-benzochrysene or a quinone of picene; unfortunately reduction yielded neither hydrocarbon. It could not be compared with the " picenequinone " of the literature, as no m. p. is recorded for this compound, or its phenazine derivative [7] [whose recorded nitrogen content (7·9%) agrees poorly with the theoretical value (7·4%; erroneously given by Meyer *et al.*[7] as 8·2%)], or for the " yellow brown precipitate " produced by reductive acetylation (whose acetyl content [7] was the only basis for its formulation as 9 : 10-diacetoxy-9 : 10-dihydro-1 : 2 : 7 : 8-dibenzophenanthrene, $C_{26}H_{20}O_4$).

The structure of the compound of m. p. 310° has, however, been determined by repeating the oxidation [4] of picene: the product was separated chromatographically into unchanged picene and a quinone identical with the Diels–Alder product which must therefore be the 5 : 6-quinone (III). There is also formed an isomeric quinone which gives a diacetoxypicene and a phenazine very much more slowly: we believe this to be the 13 : 14-quinone (II), whose quinone group would be sterically hindered. It is isolated in less than one-third the yield of the 5 : 6-quinone (III), but the amount initially formed may be much larger since excess of the oxidant (chromic acid) rapidly converts it into soluble products.

[3] Fieser and Dunn, *J. Amer. Chem. Soc.*, 1937, **59**, 1016.
[4] Bamberger and Chattaway, *Annalen*, 1895, **284**, 52.
[5] Cook, *J.*, 1941, 685.
[6] Davies, James, Middleton, and Porter, *J.*, 1955, 1565.
[7] Meyer and Hoffman, *Monatsh.*, 1916, **37**, 681.

On the other hand, the isomeric 5 : 6-quinone is only partly destroyed under these conditions and is readily oxidised to a diquinone; this is assigned the structure picene-5 : 6 : 7 : 8-diquinone, since with hydrazine hydrate it gives an azine considered to be (VII).

Experimental

3-Bromo-1 : 2-naphthaquinone, prepared by bromination [8] of 1 : 2-naphthaquinone,[9] was recrystallised from benzene immediately before use. 1-Vinylnaphthalene was made from crude 1-1'-naphthyl ethanol.[10] Picene, m. p. 365°, was a product of Rütgerswerke-Aktiengesellschaft Castrop-Rauxel 2.

Picene-5 : 6-quinone (III).—3-Bromo-1 : 2-naphthaquinone (7·3 g.) and 1-vinylnaphthalene (2·3 g.) in *sym*-tetrachloroethane (200 ml.) were heated in a boiling-water bath for 5 hr.; the solvent was then removed at reduced pressure and the oily residue triturated with acetone (50 ml.) to give crystalline *picene-5 : 6-quinone* (2·0 g.), sparingly soluble in acetone, slightly soluble in boiling benzene, or chloroform, and conveniently recrystallising from boiling xylene or acetic acid as orange-red needles, m. p. 310° (1·5 g., 33%, calc. on 1-vinylnaphthalene) (Found: C, 85·4; H, 4·0. $C_{22}H_{12}O_2$ requires C, 85·7; H, 3·9%). A slightly lower yield (30%) separated from the cooled solution when glacial acetic acid was substituted for tetrachloroethane. In cold concentrated sulphuric acid it gives a deep green, slowly changing to a permanent navy-blue, colour.

The *phenazine derivative*, yellow needles (from acetic acid), m. p. 278—278·5° (Found: N, 7·3. $C_{28}H_{16}N_2$ requires N, 7·4%), was obtained in good yield when the quinone was boiled for 15 min. with the theoretical quantity of *o*-phenylenediamine in acetic acid. It dissolves in cold concentrated sulphuric acid to a stable olive-green solution.

Oxidation of Picene.—To a suspension of picene (2·5 g.) in boiling acetic acid (200 ml.), previously distilled from chromic acid, was added chromic acid (3·2 g.) in acetic acid (100 ml.) during 10 hr. After a further 4 hours' boiling, the mixture was concentrated to 30 ml. The product was collected, washed with dilute sodium carbonate at 50°, and recrystallised from acetic acid to give ill-defined crystals, m. p. 260—280°. Sublimation of this product at 200°/0·04 mm. caused extensive decomposition and the sublimate, m. p. 270—285°, was still impure. The original product was dissolved in chlorobenzene (300 ml.) and chromatographed on deactivated silica [11] containing 7% of water. The first, colourless band was blue-fluorescent under ultraviolet light and on concentration yielded picene as colourless plates (0·07 g.), m. p. 363—365°. The eluate from the first dark brown, non-fluorescent band, on concentration, gave *picene-13 : 14-quinone* (II) (0·25 g.), red plates (from acetic acid or benzene), m. p. 285° unchanged by sublimation at 220°/1 mm. (Found: C, 85·8; H, 4·0. $C_{22}H_{12}O_2$ requires C, 85·7; H, 3·9%). It was destroyed on an attempted conversion into a diquinone under the conditions which succeeded with the isomer (III). In cold concentrated sulphuric acid there is a stable royal-blue coloration.

The second brown, non-fluorescent band was more strongly adsorbed and attempts to speed elution by addition of ethyl acetate or alcohol to the solvent resulted in precipitation of the quinone. The column was extruded and the relevant portion extracted with chlorobenzene. Concentration of the extract yielded orange needles which recrystallised from acetic acid and from benzene to give picene-5 : 6-quinone (III) (0·89 g.), m. p. 309—309·5°, unchanged by sublimation at 200°/0·002 mm. (Found: C, 85·7; H, 4·2%). The m. p. was unchanged on admixture with the previous specimen of m. p. 310°. The phenazine derivative, m. p. 278·5—278·7°, was also identical (mixed m. p.): it is difficult to burn, 50% more than the normal time being required in its combustion (Found: C, 88·0; H, 4·3. $C_{28}H_{16}N_2$ requires C, 88·4; H, 4·2%).

Reductive Acetylation of the Quinone (III).—Picene-5 : 6-quinone (0·1 g.), anhydrous sodium acetate (0·1 g.), and zinc dust (0·2 g.) were heated under reflux in acetic anhydride (5 ml.) for 1 hr. The anhydride was hydrolysed by warm water; the resulting product gave an excellent yield of *5 : 6-diacetoxypicene*, colourless needles (from benzene–light petroleum), m. p. 224—225° (Found: C, 79·3; H, 4·5; O, 16·4. $C_{26}H_{18}O_4$ requires C, 79·2; H, 4·6; O, 16·2%). Its almost colourless solution in concentrated sulphuric acid gradually became navy blue. Its solution in benzene gave a blue-violet fluorescence in ultraviolet light.

[8] Zincke, *Ber.*, 1894, **27**, 733.
[9] Fieser, *Org. Synth.*, Coll. Vol. II, p. 430.
[10] Davies and Porter, *J.*, 1957, 459.
[11] Cahnmann, *Analyt. Chem.*, 1957, **29**, 1307.

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Derivatives of Picene-13 : 14-*quinone*.—Reductive acetylation as above gave 13 : 14-*diacetoxypicene*, colourless needles (from ethanol), m. p. 236—237°, in poor yield (Found: C, 79·0; H, 4·7%). Its fluorescence resembled that of the isomer. Its sulphuric acid solution gradually became royal-blue.

The *phenazine derivative* is formed with difficulty from the quinone (0·05 g.) and *o*-phenylenediamine (0·05 g.) in refluxing acetic acid (10 ml.). Crystals appeared in 1 hr.; 0·02 g. was collected after 4 hr., and after a further 10 hr. additional phenazine (0·03 g.) separated in golden needles, m. p. 258—258·5° (from acetic acid in which it is very sparingly soluble) (Found, after extra time for combustion: C, 88·4; H, 4·2; N, 7·7%). It colours cold concentrated sulphuric acid navy-blue.

Picene-5 : 6 : 7 : 8-*diquinone*.—Chromic oxide (0·11 g.) in acetic acid was added to a boiling solution of picene-5 : 6-quinone (0·11 g.) in acetic acid (60 ml.). In about 30 seconds a precipitate of the diquinone appeared. The mixture was immediately cooled and filtered, to give the *picene*-5 : 6 : 7 : 8-*diquinone* (0·07 g.), reddish-brown needles (from *o*-dichlorobenzene), m. p. 386° (Found: C, 77·6; H, 3·2. $C_{22}H_{10}O_4$ requires C, 78·1; H, 3·0%). Its solution in cold sulphuric acid is brown and stable. It is extremely insoluble in hot acetic or heptanoic acid, and its solution in hot phenylacetic acid gave no phenazine with *o*-phenylenediamine despite apparent reaction. Under these conditions the phenazine from the monoquinone (III) is rapidly obtained in good yield after subsequent dilution with alcohol.

6 : 7-*Diazabenzo*[fgh]*picene*-5 : 8-*quinone* (VII) was formed when the diquinone (0·07 g.) was heated under reflux for 1½ hr. in pyridine (7 ml.) with 90% hydrazine hydrate (0·7 ml.); the deep blue reaction mixture was cooled and the precipitate recrystallised from boiling nitrobenzene as brown-violet needles, m. p. >450° (Found: N, 8·5. $C_{22}H_{10}O_2N_2$ requires N, 8·4%). Its solution in cold concentrated sulphuric acid is dark green, its smear is brown-violet, and its solution in organic solvents, in which it is very sparingly soluble, is orange-brown.

One of us (B. C. E.) thanks the Vacuum Oil Co. Pty. Ltd. for a scholarship. The microanalyses were carried out by Dr. Zimmermann and his staff.

UNIVERSITY OF MELBOURNE, AUSTRALIA. [*Received, October 28th*, 1958.]

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187. *Free-radical Substitution in Aliphatic Compounds. Part I. Halogenation of* n-*Butane and* iso*Butane in the Gas Phase.*[1]

By P. C. ANSON, P. S. FREDRICKS (in part), and J. M. TEDDER.

Butane and *iso*butane have been fluorinated, chlorinated, and brominated in the gas phase over a range of temperature. The relative rates of substitution of the different hydrogen atoms is in the expected order tertiary > secondary > primary in each case, and the reaction selectivity decreases in the order bromination ≫ chlorination > fluorination. The results permit a semiquantitative comparison.

THE principal reaction of aliphatic hydrocarbons is substitution by a free-radical process involving the initial formation of an alkyl radical by abstraction of hydrogen. This process is vastly different from the one-stage electrophilic substitution characteristic of aromatic compounds, and unlike the latter, very little is known about the effect of changes in the structure of the aliphatic compound on the reaction. Still less is known about the effect of changing the attacking radical. It is often suggested that because aliphatic substitution is a free-radical process it will be almost unaffected by polar groups in the substrate molecule, and that almost random attack may be expected. This is not borne out by available data, and probably authors are thinking solely about chlorination, where the activation energy of the all-important hydrogen-abstraction step is probably little over 1 kcal. mole^{-1}, whether primary, secondary, or tertiary hydrogen is removed,[2] so that near-random substitution is hardly surprising. With less reactive radicals aliphatic substitution

[1] Presented in part to the XV Congress of Pure and Applied Chemistry, Paris, 1957.
[2] Pritchard, Pyke, and Trotman-Dickenson, *J. Amer. Chem. Soc.*, 1955, **77**, 2629.

can become highly selective as is exemplified by the bromination of *iso*butane,[3] and even with chlorination purely polar effects in the molecule can have a tremendous influence (cf. 1 : 1 : 1-trifluorobutane [4]). Some aspects of this problem have been discussed recently by Brown and his co-workers.[5] In the work in the present Series it is planned to change the nature of the attacking free radical as well as the structure of the aliphatic compound so as to obtain a more detailed picture of aliphatic substitution. The reactivity of primary, secondary, and tertiary hydrogen atoms in simple aliphatic hydrocarbons as exemplified by *n*-butane and *iso*butane is now compared, fluorine, chlorine, and bromine atoms being the attacking radicals.

Previously no quantitative study of the gas-phase monofluorination of aliphatic hydrocarbons has been made although more extensive fluorination has received much attention, notably from Bigelow and his co-workers.[6] Chlorination of aliphatic compounds has received considerable attention in the semitechnical literature, but for our purposes the most important work is the classical studies of Hass, McBee, and their co-workers.[7] More recent work includes some from Russia [8] and a careful study of the chlorination of propane by Knox.[9] Bromination has received remarkably little quantitative study and the only significant papers are those by Kharasch and his co-workers,[3 10] Van Artsdalen and his co-workers,[11] and an earlier paper by Guyer and Rufer.[12] The present results and those previously reported will be compared below.

Initially we tried to start with the hydrocarbon in the liquid phase.[13] Unfortunately fluorination under these conditions was heterogeneous and relatively uncontrolled, so after a preliminary study had been made liquid-phase work was abandoned. In the gas phase the great difficulty is the control of the temperature in the highly exothermic reactions. Control was achieved by using a continuous-flow apparatus and diluting the reactants with a vast excess of nitrogen.

Experimental

Two gaseous streams, one of butane and nitrogen, and the other of the halogen and nitrogen, were preheated separately to the intended reaction temperature and then brought together in a heated reaction chamber. When necessary the dissociation of the halogen was promoted by visible and/or ultraviolet light. After passing through the chamber the gas stream continued through two packed columns to remove the unchanged halogen and the hydrogen halide formed, then through a trap maintained at −70° in which the products and the unchanged butane condensed. Samples of liquid were then withdrawn from the trap for injection into a gas-phase chromatography column which was used for the separation and estimation of the components of the product.

Apparatus.—Two similar reaction vessels were constructed, one of glass surrounded by a vapour jacket and one of copper which fitted into an electric furnace. They consisted of two preheating coils (6 mm. O.D. tubing; total volume 25 c.c. each), a mixing vessel (75 c.c.), and a subsequent coil (25 c.c.). With flow rates of 170 c.c./min. as used for the fluorinations this gives a contact time of 0·59 min. All tubing subsequent to the reaction vessel was blacked-out.

Gas-phase Chromatography.—This used apparatus essentially similar to that described previously.[13] Two columns were used: a short one (3 ft.) of wide bore (12 mm.) and a longer

[3] Kharasch, Hered, and Mayo, *J. Org. Chem.*, 1941, **6**, 818.
[4] Henne and Hinkamp, *J. Amer. Chem. Soc.*, 1945, **67**, 1197.
[5] Ash and Brown, *Rec. Chem. Progr.*, 1948, **9**, 81; Brown and Ash, *J. Amer. Chem. Soc.*, 1955, **77**, 4019; Brown and Russell, *ibid.*, 1955, **77**, 4025.
[6] Bigelow *et al.*, *J. Amer. Chem. Soc.*, 1937, **59**, 198 and many succeeding papers.
[7] Hass, McBee, and Weber, *Ind. Eng. Chem.*, 1935, **27**, 1190; 1936, **28**, 333.
[8] Tischenko and Chibakov, *Zhur. obschei Khim.*, 1937, **7**, 658, 897; Tischenko and Zhokhovets, *ibid.*, 1948, **18**, 43; Krentsel and Pokotilo, *Zhur. priklad. Khim.*, 1951, **24**, 727; Nekrasova, *Doklady Akad. Nauk S.S.S.R.*, 1953, **88**, 73, 475.
[9] Knox, *Chem. and Ind.*, 1955, 1631.
[10] Kharasch, Yu Cheng Liu, and Nudenberg, *J. Org. Chem.*, 1955, **20**, 680.
[11] Eckstein, Scheraga, and Van Artsdalen, *J. Chem. Phys.*, 1954, **22**, 28.
[12] Guyer and Rufer, *Helv. Chim. Acta*, 1940, **23**, 533.
[13] Anson and Tedder, *J.*, 1957, 4390.

one (12 ft.), somewhat narrower (6 mm.). Both were packed with " dinonyl phthalate " on Celite as before. The greatest difficulty was the separation of the fluorinated butanes from the vast excess of unchanged butane. To obtain peaks for the fluorobutanes of sufficient size for accurate estimation so much unchanged butane had to be introduced that the chromotography columns became overloaded, causing the butane peak to trail badly. This difficulty was partly overcome by using the two columns in series. The mixture of products was injected into the short, wide-bore column, the exit of which led through a trap cooled in liquid nitrogen and into the long column. The mixture was partially separated on the first column, and the unchanged butane, eluted first, was condensed in the trap and only the carrier nitrogen passed through into the second column. After most of the butane had been eluted from the first column, but before any of the fluorobutanes appeared, the trap was by-passed so that all subsequent material emerging from the short column now passed directly into the long narrow column. The second column was not now overloaded and satisfactory separation could be obtained even with the products from the fluorination of *iso*butane. Although the short column was originally intended solely for this purpose it was found suitable for the direct separation of the high-boiling bromides.

Fluorination.—A large number of preliminary runs were carried out with *n*-butane with different concentrations of reactants and both glass and copper vessels (the etching of the glass one was very slight). The products of the reaction was not altered by changing from one vessel to the other. Finally a series of runs was completed in the copper vessel at 25° (23 runs) and at 186° (24 runs) with the relative concentrations *n*-butane (5 parts), fluorine (0·75 parts, estimated from the current supplied to the generator, it being assumed to be 75% efficient), and nitrogen (180 parts). The total flow rate was 180 c.c./min. A similar series of runs was completed with *iso*butane at 25° (27 runs) and at 125° (24 runs). Temperatures above 186° were not attempted with *n*-butane because it was found that synthetic mixtures of 1-fluoro- and 2-fluoro-butane were decomposed. With *iso*butane, the reaction products when recycled through the vessel underwent thermal decomposition at much lower temperatures and for this reason the runs at 125° have little meaning. Hydrogen fluoride catalyses the decomposition of alkyl fluorides, but the high dilution and flow technique helped to minimise this effect.

Chlorination.—Chlorinations were carried out entirely in the glass vessel with two 100 w lamps for illumination. A series of runs with *n*-butane was made at −10° (12 runs), 10° (7 runs), 35° (19 runs), 80° (13 runs), and at 146° (20 runs). The relative concentrations were *n*-butane (15 parts), chlorine (1 part) and nitrogen (180 parts), with total flow rates of either 60 c.c./min. or 100 c.c./min. (these slight changes in flow had no effect on the reaction). Three runs were made at 35° with twice as much nitrogen and a total flow rate of 150 c.c./min. These again did not differ within experimental error from those at the higher concentration. *iso*-Butane was chlorinated under the same conditions at −10° (12 runs), 35° (16 runs), 80° (10 runs), and 146° (14 runs).

Bromination.—Bromination required slightly different techniques. Bromine was introduced into the gas stream by passing nitrogen through a bubbler, containing the bromine, and surrounded by a constant-temperature bath. The concentration of bromine in the gas stream was controlled by the temperature in the bath, and estimated from the known values of its vapour pressure. Because of the selective nature of the reaction it was not possible to estimate directly the relative areas of the peaks of *n*- and *iso*-butane on the same chromatogram (the actual ratio was about 1 : 60). Two different methods were employed. In the first, two chromatograms were made for each run, one with sufficient product to give a good secondary peak and the other with ten times as much material from which the primary peak could be estimated. In the second method a single chromatogram was made for each run but as soon as the *sec.*-butyl bromide had been eluted the sensitivity of the detecting recorder was increased by removing a shunt of known resistance. The ratios obtained by the two methods were, within experimental error, the same. All brominations were performed in the glass vessel illuminated by two 100 w lamps (in some runs these were supplemented by an ultraviolet lamp and in one run replaced by two 50 w lamps without affecting the ratio of the products). Runs were made at 146° (9 runs by each method). At higher temperatures there was some breakdown of products and at lower temperatures the reaction became too selective even for the above techniques. The relative concentrations of the reactants were butane (5 parts), bromine (0·5—1 part), nitrogen (80 parts), and a total gas flow of 85 c.c./min. Bromination of *iso*butane was too selective for either of the above techniques, the ratio of *iso*butyl bromide to *tert.*-butyl bromide being of the order of 1 : 200. To have sufficient material to give a measurable peak for

*iso*butyl bromide on the chromatogram meant that the column was overloaded with *tert.*-butyl bromide which, being eluted first, then trailed, making accurate estimation of the *iso*butyl bromide impossible. Butane and *iso*butane were therefore brominated competitively, and rates of formation of *tert.*-butyl bromide and of *sec.*-butyl bromide compared. Since the relative rates of bromination of primary and secondary hydrogen atoms were already known from the experiments with *n*-butane, it was possible to calculate the difference in rate of formation of *iso*- and *tert.*-butyl bromide by assuming the hydrogen atoms in *n*-butane and *iso*butane to react similarly. Six competitive runs were made at 160° with the relative concentrations *n*-butane (3 parts), *iso*butane (3 parts), bromine (1 part), nitrogen (120 parts), and a total flow of 125 c.c./min.

Discussion

The three types of halogenation may be considered to proceed by an identical process.

$$X_2 \longrightarrow 2X\cdot \quad . \quad . \quad . \quad . \quad (1)$$
$$X\cdot + RH \longrightarrow R\cdot + HX \quad . \quad . \quad (2)$$
$$R\cdot + X_2 \longrightarrow RX + X\cdot \quad . \quad . \quad (3)$$
$$2X\cdot + M \longrightarrow X_2 + M \quad . \quad . \quad (4)$$
$$2R\cdot + M \longrightarrow R_2 + M \quad . \quad . \quad (5)$$
$$R\cdot + X\cdot + M \longrightarrow RX + M \quad . \quad . \quad (6)$$

However the thermochemistry of these steps is vastly different. Assuming D(R–H) to be approximately 100 kcal. mole^{-1}, and taking the best values for the other relevant bond dissociation energies,[14] we obtain the heats of reaction in Table 1. The importance of the

Table 1. *Approximate heats of reaction (kcal. mole^{-1}) for aliphatic halogenation.*

X = F	$\Delta H_2 \gtrsim -34{\cdot}0$	$\Delta H_3 \sim -68{\cdot}0$
X = Cl	$\Delta H_2 \gtrsim -3{\cdot}0$	$\Delta H_3 \gtrsim -23{\cdot}0$
X = Br	$\Delta H_2 \gtrsim +12{\cdot}5$	$\Delta H_3 \gtrsim -23{\cdot}0$

enormous overall heat of reaction (*ca.* 100 kcal. mole^{-1}) in the case of fluorine, compared with *ca.* 25 kcal. mole^{-1} for chlorine and 10 for bromine, when attempting controlled fluorination has been discussed previously.[15] These figures also show that reaction (2) may be expected to be reversible in bromination and possibly also in chlorination, but is unlikely to be in fluorination.

In our investigation the total extent of halogenation was never allowed to exceed 15%, so the formation of polyhalogenation products can be neglected and the ratio of the two products, *e.g.*, *sec.*-butyl chloride : *n*-butyl chloride, can be equated with the rates of substitution at the primary and secondary hydrogen atoms. Steady-state conditions being assumed, and provided that recombination of the halogen atoms is the only important chain-termination step,* then the ratio of these rates multiplied by the inverse ratio of the number of hydrogen atoms of each type (Relative Selection, RS), is equal to the ratio of the rate constants k_2 for the different types of hydrogen atom (p, s, t = primary, secondary, tertiary):

$$\frac{[Bu^sX]}{[Bu^nX]} \times \frac{3}{2} = RS_p{}^s = \frac{k_2{}^s}{k_2{}^p}$$

Combining all the individual readings by the usual "least squares" procedure, we obtain $k_2{}^s/k_2{}^p = 1{\cdot}8 \exp(480 \pm 70 \text{ cal./}\boldsymbol{RT})$ for chlorination and a very tentative $k_2{}^s/k_2{}^p = 1{\cdot}1 \exp(97 \pm 20 \text{ cal./}\boldsymbol{RT})$ for fluorination.

At 398° K fluorination of *iso*butane appears to have an RS value less than unity. This

* The essential assumption here is that $k_3 \gg k_2$. Then $[R\cdot] \ll [X\cdot]$ and if k_5 and k_6 are not too large compared with k_4, only reaction 4 will be important:

$$d[RX]/dt = k_3[R\cdot][X_2]$$

By the usual steady-state assumption this becomes

$$d[RX]/dt = k_2[RH]\sqrt{(k_1/k_4[M])}$$

Thus for competitive halogenation of RH and R′H

$$[RX]/[R'X] = (k_2/k_2')/([RH]/[R'H])$$

[14] Cottrell, "Strengths of Chemical Bonds," Butterworths Scientific Publications, London, 1954.
[15] Tedder, *Chem. and Ind.*, 1955, 508.

TABLE 2. RS_p^s (*mean*) *for halogenation of* n-*butane.*

Temp. (°K)	F	Cl	Br
263		4·29 ± 0·12	
283		4·07 ± 0·17	
298	1·25 ± 0·19		
308		3·89 ± 0·30	
353		3·63 ± 0·15	
398			
419		3·34 ± 0·21	82 ± 15
459	1·18 ± 0·14		

TABLE 3. RS_p^t (*mean*) *for halogenation of* iso*butane.*

F	Cl	Br
	5·84 ± 0·13	
1·39 ± 0·16		
	5·16 ± 0·31	
	4·51 ± 0·18	
(0·98)		
	3·93 ± 0·09	1640 ± 300

is not so: at 398° K the products of the reaction are unstable. Combining the individual chlorination readings we obtain $k_2^t/k_2^p = 2{\cdot}1 \exp(540 \pm 70 \text{ cal.}/\boldsymbol{R}T)$.

Qualitatively the results are as expected and agree well with previous work. Quantitatively the chlorination results are very close to those of Knox who chlorinated propane by a static method. They differ slightly from the original work of Hass and McBee [6] presumably for the reasons discussed by Knox. Kharasch [3] and Van Artsdalen,[11] using far less sensitive analytical techniques, only detected *tert.*-butyl bromide as monobromination product of *iso*butane, which is hardly surprising in view of our results. Two recent papers report the attack of CH_3 and CD_3 radicals on propane, *iso*butane, and *n*-butane;[16 17] the results fit in well with ours.

TABLE 4. *Selectivity of different radicals* X· *for primary, secondary, and tertiary hydrogen atoms.*

	RS *at* 300° K			*Differences (cal. mole*$^{-1}$*) in activation energy*		
	$-CH_3$	$>CH_2$	$\geqslant CH$	$E_2^p - E_2^s$	$E_2^p - E_2^t$	E_2^p *
X = F	1	1·2	1·4	90	—	?
X = Cl	1	3·9	5·1	480	540	1000
X = CD_3	1	35	—	2100	—	11,000
X = CH_3	1	—	—	2300	2900	11,400
X = Br	1	82 †	1600 †	—	—	14,000

* Except for CD_3 radicals where E_2^p for butane was determined directly, these values are those reported for the corresponding reaction with ethane [Cl· + C_2H_6 (ref. 2); CH_3· + C_2H_6 (Trotman-Dickenson, Birchard, and Steacie, *J. Chem. Phys.*, 1951, **19**, 161); Br· + C_2H_6 (Andersen and Van Artsdalen, *J. Chem. Phys.*, 1944, **12**, 478)]. † RS values for bromination at 400° K.

Table 4 shows how the different radicals form a very consistent overall picture, and it suggests that E_2^p for fluorination is about 0·5 kcal. mole^{-1} or less. The only anomaly occurs in the ratios of the frequency factors A_2^s/A_2^p. For chlorination our work and that of Knox give a value of approximately 2 for this ratio, but fluorination gives a value of approximately unity, although this value is not very definite. For hydrogen abstraction by CD_3 radicals McNesby and Gordon get a value of exactly unity. The only apparent difference in the $\Delta S^\ddagger$ term would be due to a difference in symmetry factors. Approximate calculations indicate that the ratio should be greater than unity, as we have found for chlorination, but clearly further work is required.

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DEPARTMENT OF CHEMISTRY,
UNIVERSITY OF SHEFFIELD.

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[16] McNesby and Gordon, *J. Amer. Chem. Soc.*, 1956, **78**, 3570.
[17] Rice and Vanderslice, *J. Amer. Chem. Soc.*, 1958, **80**, 292.

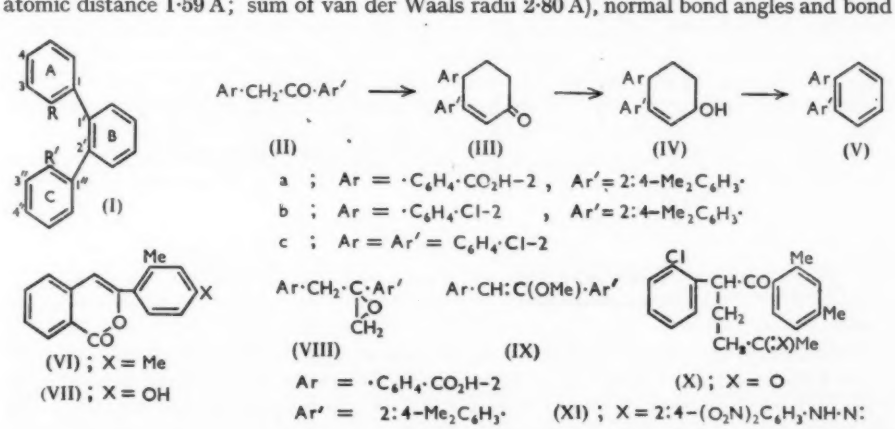
188. *Synthetical Experiments in the* o-*Terphenyl Series. Part II.*[1]

By R. L. Huang and Kheng-Hoon Lee.

Of attempted syntheses of the *o*-terphenyls (V) *via* the *cyclo*hexenones (III), the first two broke down at intermediate stages, while the third yielded a glass, probably (Vc). Preparative methods have been worked out for the intermediate deoxybenzoins and some of their properties are reported.

In a 2 : 2″-disubstituted *o*-terphenyl (I), the non-planarity of the benzene rings[2,3] could give rise to geometrical isomers in which substituents R and R′ are *cis* or *trans* to each other with respect to the central ring. An attempt to substantiate this postulate was made by synthesis[1] of the *o*-terphenyl (I; R = R′ = OMe), but only one form could be isolated. This failure could be due to either (*a*) the existence of a preferred form, or (*b*) insufficient restriction of rotation as a result of the relatively small size of the methoxyl group. This paper now reports attempts to synthesise *o*-terphenyls with bulkier *ortho*-substituents such as chloro-, carboxy-, and methyl groups.

Estimates suggest that for the 2 : 2″-dichloro-derivative (I; R = R′ = Cl), for instance, in the rotation of ring A about the pivot bond, interference is considerable between a chlorine atom at $C_{(2)}$ and the hydrogen atom at $C_{(6')}$, when rings A and B becomes co-planar (interatomic distance 1·59 Å; sum of van der Waals radii 2·80 Å), normal bond angles and bond



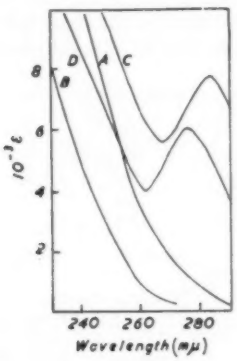
lengths[3-5] being assumed. Similarly, the interference between the same chlorine atom and ring C, even when at a minimum (which is the case when ring C is at right angles to B) is still considerable (1·25 Å and 3·59 Å, respectively). Thus, it appears probable that, unless large distortion of bond angles can occur, the geometrical isomers of 2 : 2″-dichloro-*o*-terphenyl should be stable entities.

Relatively few methods are available for the synthesis of *ortho*-substituted *o*-terphenyls. The Ullmann reaction gives low yields,[6] and moreover the high reaction temperature appears unsuitable for synthesis of isomers which might be thermally labile. The route *via* a 2-aryl*cyclo*hexanone did not give promising results,[1] while the approach involving

[1] Huang, *J.*, 1954, 3655, is considered as Part I of this series.
[2] See Pickett, Walter, and France, *J. Amer. Chem. Soc.*, 1936, **58**, 2296; Clews and Lonsdale, *Proc. Roy. Soc.*, 1937, *A*, **161**, 493; Merkel and Wiegand, *Z. Naturforsch.*, 1948, **3***b*, 93.
[3] Brockway and Karle, *J. Amer. Chem. Soc.*, 1944, **66**, 1974.
[4] Adams and Yuan, *Chem. Rev.*, 1933, **12**, 261.
[5] Brockway and Robertson, *J.*, 1939, 1329; Robertson, *Sci. Progress*, 1939, **33**, 666; Robertson, "Organic Crystals and Molecules," Cornell Univ. Press, Ithaca, N.Y., 1953, p. 227.
[6] Sadler and Powell, *J. Amer. Chem. Soc.*, 1934, **56**, 2650; Shuttleworth, Rapson, and Stewart, *J.*, 1944, 71; cf. Bachmann and Clark, *J. Amer. Chem. Soc.*, 1927, **49**, 2089.

homolytic arylation [7] by a substituted *o*-diphenylyl radical has yet to be investigated. A method which has achieved considerable success [8] and was used in the synthesis of the dimethoxy-derivative [1] makes use of a modified Robinson–Mannich synthesis from a deoxybenzoin (II) to give the diaryl*cyclo*hexenone (III). This is reduced to the alcohol (IV), then dehydrated and dehydrogenated to the terphenyl (V). This scheme, when used for the terphenyls (Va) and (Vb), broke down at intermediate stages, although practical preparative methods have been developed for the intermediates (IIa) and (IIb). In the case of the 2 : 2″-dichloro-compound, (Vc), the synthesis was carried through, but the product could not be obtained crystalline.

m-Xylene was acylated by homophthalic anhydride in the presence of aluminium chloride to the deoxybenzoin (IIa) in good yield. The presence of the *p*-methyl group, though of no steric significance in the ultimate product (Va), served here to ensure unambiguity in the course of acylation. Before use of the Robinson–Mannich reaction, the carboxyl group had to be esterified. However, ethanol and sulphuric acid converted the deoxybenzoin into the lactone (VI), while ethereal diazomethane produced a mixture of the same lactone and an acid, probably (VIII) or (IX). Since infrared absorption of the deoxybenzoin (in Nujol) showed an inflected peak at 5·9 μ (carbonyl absorption, ketone



A, 2 : 2″-*Dichloro*-o-*terphenyl* (?).
B, 2 : 2′-*Dichlorodiphenyl*.
C, 2 : 2″-*Dimethoxy*-o-*terphenyl*.
D, 2 : 2′-*Dimethoxydiphenyl*.

and acid mixed) but no hydroxy-band in the 3 μ region, it probably exists in the solid state in the ketonic, rather than the enolic form, so that enolisation had occurred by acid catalysis, and by the action of diazomethane, and this was followed by lactonisation. An analogy for the acid catalysis is found in the direct synthesis of the *iso*coumarin (VII) from homophthalic anhydride and *m*-cresol in the presence of stannic chloride.[9]

The deoxybenzoin (IIb) was prepared from *m*-xylene and *o*-chlorophenylacetyl chloride, a modification of Perrier's method [10] being adopted. The preparation of *o*-chlorophenylacetic acid through *o*-chlorobenzaldehyde cyanohydrin [11] did not prove promising, but the route *via* the oxazolone and *o*-chlorophenylpyruvic acid gave satisfactory results.[12] The pyruvic acid was unstable, decomposing readily into *o*-chlorobenzaldehyde.

Condensation of the above ketone with 4-diethylaminobutan-2-one in the presence of sodium ethoxide gave, not the expected *cyclo*hexenone (IIIb), but the open-chain diketone (X) isolated as a mono-2 : 4-dinitrophenylhydrazone. To this the ketonic structure (XI) is assigned since its infrared spectrum (in Nujol) exhibits the peak at 6·0 μ characteristic of an aryl ketone, and no hydroxyl peak in the 3 μ region. As variation of conditions

[7] *E.g.*, see Cadogan, Hey, and Williams, *J.*, 1954, 3352.
[8] Dodds, Huang, Lawson, and Robinson, *Proc. Roy. Soc.*, 1953, *B*, **140**, 470.
[9] Buu Hoï, *Bull. Soc. chim. France*, 1944, **11**, 338.
[10] Perrier, *Ber.*, 1900, **33**, 815.
[11] Levine, Eble, and Fishbach, *J. Amer. Chem. Soc.*, 1948, **70**, 1930.
[12] Cf. *Org. Synth.*, Col. Vol. II, p. 55; Adams, "Organic Reactions," Vol. III, pp. 209, 225.

XUM

in the Robinson–Mannich reaction did not bring about cyclisation, and as attempts to cyclise the open-chain ketone (X) with potassium *tert.*-butoxide and with hydrogen bromide in acetic acid [8] were unsuccessful, the synthesis of the terphenyl (IIb) was not pursued.

The preparation of 2 : 2′-dichlorodeoxybenzoin by reaction of an excess of *o*-chlorophenylmagnesium bromide with *o*-chlorobenzamide, reported by Jenkins and Richardson [13] to give a 70% yield, afforded only 34% of the product accompanied by considerable quantities of 2 : 2′-dichlorodibenzyl, despite variations of conditions. An alternative route, *via* the benzoin condensation [14,15] of *o*-chlorobenzaldehyde followed by reduction, was next examined. An adaptation of Lutz and Murphey's method [16] gave a higher yield of the benzoin, which was directly oxidised to the benzil (49% overall). This on reduction with hydriodic acid gave not the deoxybenzoin as would be expected by analogy with benzil and certain substituted benzils,[17] but 2 : 2′-dichlorobenzoin (69%). Reduction with tin–copper couple [18] gave the required deoxybenzoin in 83% yield, and in a much purer form than that obtained by Jenkins and Richardson's method. Reduction by the same method of the product from the above benzoin condensation gave an inseparable mixture probably of 2 : 2′-dichloro-hydrobenzoin and -deoxybenzoin, which gave the benzil by oxidation with nitric acid.

The 2 : 2′-dichlorodeoxybenzoin condensed with methyl vinyl ketone (Robinson–Mannich synthesis) to furnish the *cyclo*hexenone (IIIc). Pondorff reduction of this ketone gave the *cyclo*hexenol (IVc), or an isomer thereof, dehydration occurring readily with potassium hydrogen sulphate in boiling cumene (though sluggishly in refluxing benzene). The diene so obtained was directly dehydrogenated with palladised charcoal to a glass, probably 2 : 2″-dichloro-*o*-terphenyl, which could not be induced to crystallise. This tendency to supercool has been noted in *o*-terphenyl itself [19] and is attributed to interlocking of molecules in the crystal. The ultraviolet absorption of the product, measured in hexane, possesses characteristics very similar to that of 2 : 2′-dichlorodiphenyl [20,21] (see Figure), a resemblance also shown between 2 : 2″-dimethoxy-*o*-terphenyl [1] and 2 : 2′-dimethoxydiphenyl.[20]

Experimental

2′-Carboxy-2 : 4-dimethyldeoxybenzoin.—*m*-Xylene (14 g.) in tetrachloroethane (*ca.* 25 c.c.) was added during 15 min. to a well-stirred mixture of homophthalic anhydride [22] (10·5 g.) and powdered aluminium chloride (20 g.) in the same solvent (150 c.c.). The mixture was stirred for 24 hr., poured on chipped ice, and after addition of concentrated hydrochloric acid (30 c.c.) was heated to 70° for 30 min. The organic layer was separated, the aqueous layer extracted with ether, and the combined organic solution washed with water, and extracted 3 times with 10% aqueous sodium hydroxide. The alkaline extract, after being washed with ether, was acidified with dilute hydrochloric acid, and the precipitate taken up in ether. Removal of the solvent then gave the required *deoxybenzoin* (9·5 g., 54% yield), m. p. 135—136° after crystallisation from benzene–*cyclo*hexane (Found: C, 76·2; H, 6·2. $C_{17}H_{16}O_3$ requires C, 76·1; H, 6·0%). It dissolved readily in 10% aqueous sodium hydrogen carbonate.

Attempted Esterification.—(*a*) The deoxybenzoin (7·5 g.) was refluxed with ethanol (80 c.c.) containing sulphuric acid (5·6 g.) for 12 hr. Most of the alcohol was removed under reduced pressure, and the residue poured on ice containing sodium hydrogen carbonate just sufficient to neutralise the sulphuric acid. The organic matter was taken up in ether, washed with water,

[13] Jenkins and Richardson, *J. Amer. Chem. Soc.*, 1933, **55**, 1618.
[14] Hodgson and Rosenberg, *J.*, 1930, 14; Weissberger, Strasser, Mainz, and Schwarz, *Annalen*, 1930, **478**, 112; Gilman and Broadbent, *J. Amer. Chem. Soc.*, 1948, **70**, 2619.
[15] Cf. *Org. Synth.*, Col. Vol. I, p. 87.
[16] Lutz and Murphey, *J. Amer. Chem. Soc.*, 1949, **71**, 478.
[17] Japp and Klingemann, *J.*, 1893, **63**, 770; Fuson, Armstrong, Chadwick, Kneisky, Rowland Shank, and Soper, *J. Amer. Chem. Soc.*, 1945, **67**, 386; Fuson and Hoch, *ibid.*, 1949, **71**, 1585.
[18] Allen and Buck, *J. Amer. Chem. Soc.*, 1930, **52**, 310.
[19] Andrews and Ubbelohde, *Proc. Roy. Soc.*, 1955, *A*, **228**, 435.
[20] Williamson and Rodebush, *J. Amer. Chem. Soc.*, 1941, **63**, 3018.
[21] Bastiansen, *Acta Chem. Scand.*, 1950, **4**, 926.
[22] *Org. Synth.*, Col. Vol. II, p. 449.

dried, and concentrated. The crystalline residue was crystallised from ethanol, giving **3-(3 : 4-*dimethylphenyl*)iso*coumarin*** as long needles (3·7 g.), m. p. 120·5—121·5° after several recrystallisations (Found: C, 81·6; H, 5·8. $C_{17}H_{14}O_2$ requires C, 81·6; H, 5·6%).

(*b*) An ice-cold solution of diazomethane in dry ether (prepared from 10·3 g. of methylnitrosourea) was added portionwise to a solution of the deoxybenzoin (15·0 g.) in dry ether (*ca.* 250 c.c.) at 20°. Next day, the solution was extracted twice with 10% aqueous sodium hydrogen carbonate and the aqueous and ethereal solutions were worked up separately as follows. (i) The aqueous solution was acidified, and precipitated organic matter isolated by ether extraction, giving a crystalline *compound* (4·7 g.), hexagonal prisms, m. p. 129—130° after crystallisation from light petroleum–benzene (Found: C, 76·3; H, 6·1. $C_{18}H_{18}O_3$ requires C, 76·6; H, 6·4%). It did not react with 2 : 4-dinitrophenylhydrazine. (ii) The ethereal solution was washed with water, dried, and concentrated, and the residue (10·8 g.) distilled to give a viscous orange liquid, b. p. 186—192°/0·8 mm. (7·6 g.), which partially crystallised, giving the *iso*coumarin obtained previously, m. p. and mixed m. p. 120—121° (Found: C, 81·6; H, 5·6%).

o-*Chlorophenylacetic Acid.*—The oxazolone (75 g.; m. p. 158—159°) prepared from *o*-chlorobenzaldehyde and hippuric acid by Mauthner's method [23] was boiled with 10% aqueous sodium hydroxide (1200 c.c.) for 5 hr. under nitrogen. The solution was cooled in ice and vigorously stirred while 10% hydrogen peroxide (380 c.c.) was added during ½ hr. Next day, 6N-hydrochloric acid was added, and the precipitate filtered off. Benzoic acid was removed by prolonged steam-distillation, and the *o*-chlorophenylacetic acid, which remained in the residue, crystallised repeatedly from light petroleum (b. p. 60—80°), m. p. 93—94° (12·1 g., 27%). Campbell and McKail [24] report m. p. 93—95°. An attempt to isolate *o*-chlorophenylpyruvic acid from the hydrolysis products of the oxazolone, Perkin's sulphur dioxide method being used,[25] yielded only *o*-chlorobenzoic acid (odour of aldehyde).

2′-*Chloro*-2 : 4-*dimethyldeoxybenzoin.*—Crude *o*-chlorophenylacetyl chloride [from the acid (12·0 g.)] was added to a stirred mixture of powdered aluminium chloride (10·0 g.) and *sym*-tetrachloroethane (75 c.c.). When all the aluminium chloride had dissolved (*ca.* 20 min.), *m*-xylene (12·5 c.c.) in the same solvent (25 c.c.) was added during 1 hr., the mixture being kept at room temp. (28°). Stirring was continued for 2 hr. more, and the mixture then poured on ice. Next day, concentrated hydrochloric acid (20 c.c.) was added, the organic layer was separated, and the aqueous layer extracted with tetrachloroethane. The combined organic solution was washed with water, aqueous sodium hydrogen carbonate, and water, and dried. On removal of the solvent under reduced pressure the ***deoxybenzoin*** (16·5 g.) separated. It crystallised from methanol in needles, m. p. 90—90·5° (Found: C, 74·4; H, 5·9; Cl, 14·2. $C_{16}H_{15}OCl$ requires C, 74·3; H, 5·8; Cl, 13·7%). The **2 : 4-*dinitrophenylhydrazone***, orange-coloured leaflets from ethanol–ethyl acetate, had m. p. 234—235° (Found: N, 12·5. $C_{22}H_{19}O_4N_4Cl$ requires N, 12·7%).

Robinson–Mannich Reaction.—The above deoxybenzoin (4·0 g.) in dry benzene (30 c.c.) was added at 5—10° to the methiodide prepared from methyl iodide (2·4 g.) and 4-diethylaminobutan-2-one [26] (2·4 g.), under nitrogen. Sodium ethoxide [from sodium (0·8 g.)] in ethanol (30 c.c.) was then added in two equal portions, the first during 30 min. and the second during 10 min. The mixture was kept at *ca.* 10° for 1 hr., then heated slowly, and finally refluxed gently for 15 min. It was poured on chipped ice containing a slight excess of sulphuric acid, and the organic matter isolated with ether. The extract, after being washed with aqueous solutions of sodium hydrogen sulphite and of sodium hydrogen carbonate, and with water, was dried, concentrated, and distilled with benzene until the ethanol was completely removed. The residue was then adsorbed on alumina and eluted with benzene. When distilled under nitrogen it gave a pale yellow oil, b. p. 176—185°/0·5 mm. (*ca.* 3·6 g.), which failed to crystallise. With Brady's reagent it gave **2-o-*chlorophenyl*-1-(2 : 4-*dimethylphenyl*)*hexane*-1 : 5-*dione mono*-2 : 4-*dinitrophenylhydrazone***, m. p. 147—148° after crystallisation from ethanol–ethyl acetate (Found: C, 61·1; H, 5·0. $C_{26}H_{25}O_5N_4Cl$ requires C, 61·3; H, 4·95%). A portion of the distillate slowly crystallised, and proved to be unchanged deoxybenzoin. However, further distillation failed to give the diketone pure. Variation of conditions by (*a*) using potassium ethoxide or *tert.*-butoxide instead of sodium ethoxide, and (*b*) increasing the period of reflux (1—2 hr.), did not improve the results.

[23] Mauthner, *J. prakt. Chem.*, 1917, **95**, 55.
[24] Campbell and McKail, *J.*, 1948, 1251.
[25] Haworth, Perkin, and Rankin, *J.*, 1924, **125**, 1686.
[26] Wild and Shunk, *J. Amer. Chem. Soc.*, 1943, **65**, 469.

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2 : 2′-*Dichlorodeoxybenzoin.*—(*a*) *Jenkins and Richardson's method.*[13] Finely powdered *o*-chlorobenzamide (39 g.) was added in 1·5 hr. with stirring to a Grignard solution [from *o*-chlorobenzyl chloride (161 g.) and magnesium (24·3 g.)] in ether (*ca.* 500 c.c.) under nitrogen. The stirred mixture was heated under reflux for 50 hr., then poured on ice containing dilute sulphuric acid, and the product was extracted into ether, and worked up in the usual way. Distillation through a 15-cm. Vigreux column under nitrogen gave fractions: (i) *o*-chlorotoluene (51 g.); (ii) 2 : 2′-dichlorodibenzyl (23·4 g.), b. p. 115—124°/0·2 mm., m. p. 62—62·5° (from methanol) (Found: C, 67·1; H, 5·0. Calc. for $C_{14}H_{12}Cl_2$: C, 66·9; H, 4·9%) (lit.[27] m. p. 65°); (iii) material (9·3 g.), b. p. 124—134°/0·2 mm., which was mostly 2 : 2′-dichlorodibenzyl; and (iv) a yellow liquid which when refractionated gave the benzoin (16·0 g.), b. p. 138—144°/0·2 mm., n_D^{20} 1·6023 (Found: Cl, 27·1. Calc. for $C_{14}H_{10}OCl_2$: Cl, 26·7%). Jenkins and Richardson [13] record b. p. 195—210°/6 mm. The 2 : 4-*dinitrophenylhydrazone* formed plates, m. p. 171—172° (from ethanol–ethyl acetate) (Found: N, 11·7. $C_{20}H_{14}O_4N_4Cl_2,C_2H_6O$ requires N, 11·4%).

Use of benzyl bromide instead of the chloride reduced the yield of ketone to only 34%.

(*b*) Crystalline 2 : 2′-dichlorobenzoin (12·8 g.; see below) was heated with granulated tin (25 g.), saturated aqueous copper sulphate (3 c.c.), and ethanol (125 c.c.) for 2·5 hr., during which time concentrated hydrochloric acid (100 c.c.) containing the same copper sulphate solution (7·5 c.c.) was added in small portions. The deoxybenzoin was then isolated by benzene extraction, and distilled; it had b. p. 154—156°/0·5 mm. (10·0 g.), n_D^{22} 1·5983.

2 : 2′-*Dichloro-benzoin and -benzil.*—(*a*) A saturated aqueous solution of potassium cyanide (1·8 g.; "AnalaR") was slowly added to a boiling solution of freshly distilled *o*-chlorobenzaldehyde (177 g.) in methanol (110 c.c.), and the mixture boiled for a further 30 min. Methanol was removed, and the residue, dissolved in benzene, was repeatedly extracted with 20% aqueous sodium hydrogen sulphite, then washed with 10% aqueous sodium hydrogen carbonate, and water, dried, and concentrated. The crude dichlorobenzoin (144 g.) could not be induced to crystallise. A portion (4·0 g.) was oxidised by copper sulphate in pyridine [15] to give 2 : 2′-dichlorobenzil, m. p. 133—134° (2·4 g.) (lit.,[28] m. p. 133—134°). Reduction of the crude dichlorobenzoin by a tin–copper couple (Allen and Buck's method [18]) gave a mixture, apparently of isomeric hydrobenzoins, which on oxidation with nitric acid (5 hr. at 100°) also gave the benzil (71% yield).

(*b*) 2 : 2′-Dichlorobenzil (31 g.), 55% hydriodic acid (250 c.c.), and acetic acid (400 c.c.) were stirred at the boiling point for 2 hr. Water was added, and the product taken up in benzene, washed with aqueous sodium hydrogen sulphite and sodium hydrogen carbonate, and water, then dried, and concentrated under reduced pressure. On distillation under nitrogen 2 : 2′-dichlorobenzoin (25·5 g.) was obtained, b. p. 160—170°/0·9 mm., needles, m. p. 62—63° [from benzene–petroleum (b. p. 60—80°)] (Found: C, 59·7; H, 3·6. Calc. for $C_{14}H_{10}O_2Cl_2$: C, 59·8; H, 3·6%) (lit.,[14] m. p. 63—64°). It was stable in air.

3 : 4-*Di*-o-*chlorophenyl*cyclo*hex*-2-*en*-1-*one.*—The above deoxybenzoin (6·0 g.) was subjected to the Robinson–Mannich reaction as previously described. The mixture, after 3·5 hr. at room temperature, was finally refluxed gently for 0·5 hr., and the product was isolated and chromatographed on alumina. The oil (5·1 g.) failed to crystallise and was distilled, giving (i) material, b. p. 158—168°/0·2 mm. (1·4 g., of which 0·9 g. separated as a solid), and (ii) the required cyclo*hexenone* (1·7 g.), b. p. 171—180°/0·2 mm., m. p. 117—118° (from light petroleum) (Found: C, 68·1; H, 4·6; Cl, 22·7. $C_{18}H_{14}OCl_2$ requires C, 68·1; H, 4·4; Cl, 22·3%). It gave a 2 : 4-*dinitrophenylhydrazone*, orange needles, m. p. 223·5—224° from ethanol–ethyl acetate (Found: N, 11·5. $C_{24}H_{18}O_4N_4Cl_2$ requires N, 11·3%). The solid which separated from fraction (i) was the same *cyclo*hexenone (total yield 2·6 g., 35%).

3 : 4-*Di*-o-*chlorophenyl*cyclo*hex*-2-*en*-1-*ol.*—The *cyclo*hexenone (2·4 g.) was heated with aluminium *iso*propoxide (10 g.) and dry *iso*propyl alcohol (50 c.c.) for 24 hr. under a fractionating column at such a rate that the acetone produced slowly distilled off. The mixture was then poured on ice and dilute hydrochloric acid, and the organic matter taken up in benzene, washed in turn with dilute hydrochloric acid, water, aqueous sodium hydrogen carbonate, and dried, and the solvent removed. The oil which remained did not react with 2 : 4-dinitrophenylhydrazine, and was absorbed on alumina and eluted first with benzene and then with benzene containing 5% of acetone, to give the cyclo*hexenol* (*ca.* 2·1 g.) which formed fine needles, m. p.

[27] Thiele and Holzinger, *Annalen*, 1899, **305**, 100.

[28] Deliwala and Rajagopalan, *Proc. Indian Acad. Sci.*, 1950, **31**, *A*, 110; cf. Gilman and Broadbent, ref. 14.

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83—85° (from petroleum) (Found: C, 68·1; H, 5·3; Cl, 22·3. $C_{18}H_{16}OCl_2$ requires C, 67·75; H, 5·0; Cl, 22·2%).

Dehydration. The *cyclo*hexenol (1·9 g.) in cumene (15 c.c.) was heated under reflux (bath temp. 170—175°) with freshly fused potassium hydrogen sulphate (1 g.) for 22 hr. under nitrogen, additional sulphate (1 g.) being introduced after the first 6 hr. Water was introduced, and the product extracted into benzene, washed with water and aqueous sodium carbonate, dried, and concentrated. Chromatography on alumina with benzene as eluent gave an oil (1·0 g.) which absorbed bromine readily; it did not crystallise and was dehydrogenated as such. Some unchanged *cyclo*hexenol was recovered in the later fractions in the chromatography.

Dehydrogenation. The crude dehydration product (0·85 g.) was boiled in cumene (15 c.c.) with 10% palladised charcoal (0·3 g.) under nitrogen for 22 hr. Benzene was added, and after filtration the solvents were completely removed under reduced pressure. The residue, in benzene, was adsorbed on alumina and eluted with the same solvent. The first 80 c.c. gave a viscous oil (0·74 g.) whilst later fractions affording negligible quantities of material. Attempts to induce the oil to crystallise failing, it was repeatedly distilled to give a glass, probably 2 : 2″-*dichloro*-o-*terphenyl* (*ca.* 0·4 g.), b. p. 144—147° (bath)/0·2 mm. (Found: C, 72·3; H, 4·1; Cl, 23·4. $C_{18}H_{14}Cl_2$ requires C, 72·2; H, 4·0; Cl, 23·7%). All attempts to induce crystallisation were unsuccessful. Dehydrogenation was repeated, in boiling ethylbenzene for 43 hr., to give material which after chromatography and distillation similarly would not crystallise.

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UNIVERSITY OF MALAYA, SINGAPORE 10. [*Received, January 30th,* 1958.]

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189. *Alkoxides as Initiators of Anionic Polymerisation of Vinyl Monomers. Part I. Polymerisation of Acrylonitrile by Use of Sodium Alkoxides.**

By ALBERT ZILKHA, BEN-AMI FEIT, and MAX FRANKEL.

Acrylonitrile was polymerised by various sodium alkoxide catalysts at low temperature in a non-polar medium. Factors and conditions of polymerisation were studied. The relative reactivity of the catalysts followed the acidity of the parent alcohol.

THE most common basic catalysts for the anionic polymerisation of vinyl monomers reported include organometallic compounds such as Grignard reagents,[1] alkali-metal alkyls,[2] alkali metals,[3] and amides of alkali metals in liquid ammonia.[1,4] Only few instances are given of the use of alkali-metal alkoxides. Ethyl crotonate [5] and allyl cyanide [6] are polymerised by sodium ethoxide and the polymerisation of acrylonitrile by sodium methoxide has been mentioned.[7]

The anionic polymerisation of vinyl monomers having electronegative groups attached to the double bond depends on the basic strength of the catalyst. Sodium alkoxides being strongly ionic were found to be very effective for the polymerisation of acrylonitrile initiated by alkoxide anions. These alkoxides have different basic strengths depending on the acidity of the hydroxyl-hydrogen atom of the alcohol. The more acidic alcohols give less basic alkoxides and therefore weaker catalysts.

* For a preliminary account of some of this work, see *Proc. Chem. Soc.*, 1958, 255.

[1] Beaman, *J. Amer. Chem. Soc.*, 1948, **70**, 3115.
[2] Hsieh and Tobolsky, *J. Polymer Sci.*, 1957, **25**, 245; Morita and Tobolsky, *J. Amer. Chem. Soc.*, 1957, **79**, 5853; Zilkha, Albeck, and Frankel, *J. Chem. Educ.*, 1958, **35**, 345.
[3] Ziegler, *Angew. Chem.*, 1938, **49**, 499.
[4] Higginson and Wooding, *J.*, 1952, 760.
[5] Pechmann, *Ber.*, 1900, **33**, 3329.
[6] Bruylants, *Bull. Soc. chim. Belg.*, 1923, **32**, 317.
[7] Bullitt, U.S.P. 2,608,554—5; *Chem. Abs.*, 1953, **47**, 1430; Schildknecht, "Polymer Processes," Interscience, New York, 1956, p. 225.

The relative acidity of the hydroxyl-hydrogen atom in alcohols depends on the chain length of the alcohol and on the position of a side chain with reference to the hydroxyl group.[8] The determining factor in the acid strength of an alcohol depends on its being primary, secondary, or tertiary owing to the inductive (+ *I*) effect of the alkyl groups, and chain length is of secondary importance. The relative acidity of various alcohols was determined by Norris and Cortese [9] from the velocity of the reaction with *p*-nitrobenzoyl chloride to be methanol > ethanol > hexan-1-ol > pentan-1-ol > butan-1-ol > propan-1-ol > benzyl alcohol > propan-2-ol > *tert.*-butyl alcohol.

From the definition of autoprotolysis constants ($K_{auto} = K_a \cdot K_b$), decrease in the acidity of the alcohol increases K_b. Thus the less acidic alcohols yield stronger catalysts.

Acrylonitrile was polymerised at low temperature (−15°) in a non-polar medium (light petroleum). The solubility of acrylonitrile in this medium was low at this temperature and two liquid phases were formed.

The dependence of yield of polymer on the amount of catalyst was studied under otherwise constant conditions with methanolic sodium methoxide (5·3N), the catalyst being added to the polymerisation mixture. Up to a certain limit, increase in amount of catalyst increased the yield (Table 1, *A*). Similar results were obtained with ethanolic sodium ethoxide (2·5N) (Table 1, *C*). Differences in yield were found if the catalyst was added in one portion (Table 1, *A*) or at intervals (Table 1, *B*). The latter gave smaller yields, especially with small amounts of catalyst owing to the small effective amount present at the start. A threshold concentration of catalyst was needed to start polymerisation. With large amounts of catalyst, the polymerisation started in a short time and was more energetic, yielding coloured polymer.

This dependence was also investigated with use of constant quantities of alcohol (Table 2). The yield increased continuously with increase in amount of catalyst (Table 2, *A*) indicating that the lowering in yield at large amounts of catalyst (Table 1) was due to

TABLE 1. *Dependence of polymerisation yield on amount of catalyst.*

([Alcohol] not kept constant.)

A. *Experimental conditions*: Methanolic solution of sodium methoxide (5·3N) was added in one portion dropwise from a pipette to cooled acrylonitrile (40 ml.)–light petroleum (b. p. 40—60°; 75 ml.). Polymerisation temperature −15°, time 120 min.

Catalyst (ml.)	1	2	3	5	6	10	15
Polymer (g.)	0	8	13·5	16	21·5	23	15·5

B. *Experimental conditions*: As in *A* except that the catalyst was added in 4 portions at intervals of 30 min.

Catalyst (ml.)	2	4	5	6	8	10	15
Polymer (g.)	0	11·5	13·5	15·5	20·5	22·5	17·5

C. *Experimental conditions*: As in *A*; ethanolic sodium ethoxide (2·5N) used as catalyst.

Catalyst (ml.)	3	5	8	10	15	20
Polymer (g.)	3·5	13	17·5	20·5	19	15·5
Induction period (min.)	16	4	4	4	3	2

the greater amount of alcohol present in the catalyst. Use of more alcohol gave respectively lower yields (cf. Table 2, *A* and *B*).

Under otherwise constant conditions, there was a continuous increase in yield with time. However most of the polymerisation was over after 90 min.; longer polymerisation time led to very small increase in yield. Thus increase in the polymerisation time from 2 to 4·5 hr. gave a 6% increase in yield while that from 30 min. to 60 min. caused about 150% increase in yield (Table 3).

The order of addition of reactants was important. Comparing the experimental conditions of Table 1 and Table 3, we see that there are great changes in yield. Addition

[8] McEwen, *J. Amer. Chem. Soc.*, 1936, **58**, 1124; Norris and Ashdown, *ibid.*, 1925, **47**, 837.
[9] Norris and Cortese, *J. Amer. Chem. Soc.*, 1927, **49**, 2640.

TABLE 2. *Dependence of polymerisation yield on amount of catalyst.*

([Alcohol] kept constant.)

A. Experimental conditions: Methanolic sodium methoxide (5·86N) was diluted with methanol to 10 ml. and added in one portion to the polymerisation mixture prepared as in Table 1. Polymerisation temp. −15°, time 90 min.

Catalyst (5·86N) (ml.)	1	2	3	4	5	7
Concn. of catalyst after diln. (N)	0·586	1·17	1·76	2·34	2·93	4·1
Induction period (min.)	—	25	8	2	2	0
Yield (g.)	0	10·5	18	18	18·5	21·5 *

* Polymerisation was very energetic and a coloured polymer (brown-red) was obtained. Greater amounts of catalyst gave still more energetic reactions.

B. Experimental conditions: As in *A*, the catalyst being diluted with methanol to 15 ml.

Catalyst (5·86N) (ml.)	2	3	5	7
Concn. of catalyst after diln. (N)	0·78	1·17	1·95	2·73
Induction period (min.)	64	36	20	1·5
Yield (g.)	9	13	14	12

TABLE 3. *Dependence of yield on polymerisation time.*

Experimental conditions: Methanolic sodium methoxide (5 ml., 5·3N) was added from a pipette in one portion to light petroleum (b. p. 40—60°; 75 ml.) cooled to −15°, and immediately followed by acrylonitrile (40 ml.). Polymerisation temp. −15°.

Time (hr.) *	0·5	1	1·5	2	2·5	3·5	4·5
Polymer (g.)	7	17·5	23	24·5	24·5	25	26

* Induction period in all experiments was about 5 min.

of the monomer to the catalyst gave greater yield than the reverse order [cf. Table 3 with Table 1 (with 5 ml. of catalyst) where 24·5 g. and 16 g. polymer were obtained, respectively].

The dependence of yield on the quantity of monomer was investigated under constant conditions (Table 4); it increased with monomer up to a limit and then decreased. It is noteworthy that use of small amounts of monomer, thus having a proportionally high concentration of catalyst, gave relatively low yields. Large quantities of monomer led to long induction periods (Table 4).

TABLE 4. *Dependence of polymerisation yield on quantity of monomer.*

Experimental conditions: Methanolic sodium methoxide (5 ml., 5·35N) was added from a pipette to cooled light petroleum (b. p. 40—60°; 75 ml.) and stirred for 5 min.; acrylonitrile was then added. Polymerisation temp. −15°, time 90 min.

Monomer (ml.)	10	20	30	40	50	60 *
Yield (g.)	5·2	11·5	18·5	26·5	24	27·5
Yield (%)	65	72	78	82	60	57

* Induction period 50 min.

Dilution of the monomer was necessary for controllable polymerisation. Addition of catalyst to undiluted monomer even at low temperatures gave violent reactions yielding red low polymers. The ratio of the amount of light petroleum to monomer affected the yield (Table 5). An optimal range of ratios was found.

TABLE 5. *Dependence of yield on amount of light petroleum.*

Experimental conditions: Methanolic sodium methoxide (5 ml.; 5·3N) was added to a cooled mixture of acrylonitrile (40 ml.) and light petroleum (b. p. 40—60°). Polymerisation temp. −15°, time 1 hr.

Light petroleum (ml.)	50	100	150
Yield (g.)	12 *	17	14·5
Induction period (min.)	8	14	13

* The polymer obtained was lightly coloured.

Temperature was important. Experiments with sodium methoxide under the conditions of Table 1 showed that below about −30° to −40° no polymerisation occurred while

temperatures higher than about −5° to 0° led to uncontrolled polymerisation yielding coloured sticky low polymers.

Using solid sodium methoxide (Matheson, U.S.A.) under otherwise constant conditions (Table 6), we obtained very low yields, showing the great difference in the catalytic reactivity as compared with methanolic sodium methoxide. However, addition of methanol to a stirred suspension of solid sodium methoxide in light petroleum followed by addition of monomer gave very high yields (Table 6). The low yields obtained with solid

TABLE 6. *Polymerisation by solid sodium methoxide.*

Experimental conditions: Solid sodium methoxide (Matheson, U.S.A.) was added to cooled light petroleum (b. p. 40—60°; 75 ml.) and stirred for 5 min. Acrylonitrile (40 ml.) was then added. Polymerisation temp. −15°, time 2 hr.

Catalyst (g.)	1·4	2·25	2·81	4·22
Equivalence to 5·2N methanolic solution (ml.)	5	8	10	15
Yield (g.)	1 *	2·5	3 †	5

* This run, stopped after 3·5, hr. gave 2 g. polymer.
† Experiment carried out with addition of 10 ml. of methanol to the suspension of the solid sodium methoxide in light petroleum. This was stirred for 5 min. and then monomer added. The yield was 20 g. of polymer.

sodium methoxide seem to be due to the surface area of the catalyst and the presence of alcohol. The latter has a solvent effect on the solid sodium methoxide, and a catalyst-activating effect which will be considered later. Precipitation of the catalyst from solution by light petroleum gave particles of much greater surface area than that of the solid sodium methoxide.

The amount of alcohol had a marked effect on the polymerisation; further experiments (Table 7) with the same amount of catalyst and various amounts of alcohol showed that the yield was greatly affected. Up to a limit, addition of alcohol increased the yield, after which a sharp drop was noticed; this shows the catalyst-activating effect and the inactivating polar effect of the alcohol. With more acidic alcohols the latter effect is more pronounced.

Comparable experiments with sodium alkoxides dissolved in the parent alcohol showed (Table 8) good agreement with the order of the basic strength of alkoxides. The strongly basic alkoxides worked even at relatively low concentrations and gave very high yields in

TABLE 7. *Effect of alcohol on the polymerisation.*

A. Experimental conditions: A constant quantity of methanolic sodium methoxide (3 ml., 5·86N) was diluted with the required quantity of methanol and added in one portion to a cooled mixture of light petroleum (b. p. 40—60°; 75 ml.) and acrylonitrile (40 ml.); polymerisation temp. −15°, time 90 min.

Methanol added to catalyst (ml.)	0	5	7	12	17
Concn. of catalyst in methanol (N)	5·86	2·19	1·76	1·17	0·88
Yield (g.)	15	19·5	19	13	5·5
Induction period (min.)	8	8	7·5	34	50

B. Experimental conditions: Methanolic sodium methoxide (5 ml.; 5·3N) was added to a cooled solution of methyl alcohol and light petroleum (b. p. 40—60°). Catalyst, stirred for 5 min. with monomer (40 ml.), was added in one portion from a pipette; polymerisation temp. −15°, time 90 min.

Added methanol (ml.)	0	10	25
Light petroleum (ml.)	75	65	50
Yield (g.)	26	13 *	0 †

* Induction period 15 min.
† Even at room temperature no polymerisation occurred.

a short time. The induction period with strong catalysts was very short. With sodium allyloxide in allyl alcohol, no polymerisation occurred: this may be due to the high acidity of allyl alcohol as shown by its strong reaction with sodium. Under basic conditions, the inductive effect (− *I*) of the double bond would dominate the resonance effect (the anionotropy of the hydroxyl group) and so enhance the acidity of the hydrogen.

TABLE 8. *Comparison of the relative reactivity of various alkoxides in the polymerisation of acrylonitrile.*

Experimental conditions: Sodium alkoxide solutions dissolved in the derived alcohol (2·5N) were added to a cooled mixture of light petroleum (b. p. 40—60°; 75 ml.) and acrylonitrile (40 ml.). Polymerisation temp. −15°.

	Catalyst 3 ml., time 60 min.		Catalyst 5 ml., time 30 min.	
Alkoxide	Yield (g.)	Induction period (min.)	Yield (g.)	Induction period (min.)
Methoxide	0	—	0 [a,b]	—
Ethoxide	2·5	16	6·5	8
n-Propoxide	0·5	—	7	4
*iso*Propoxide	—	—	explosive polym.[c]	0
Allyloxide	0	—	0 [d]	—
n-Butoxide	5·5	4	explosive polym.[c]	0
n-Pentyloxide	2·5	4	14·5 [e]	4
Benzyloxide	—	—	10·5 [f]	3

[a] The induction period was more than 30 min. This experiment carried out for 2 hr. gave 14 g. of polymer. [b] Use of methoxide catalyst (10 ml.) gave 19·5 g. of polymer after 2 hr. [c] In these "explosive reactions" the polymerisation is very fast and goes out of control. The polymer, as fine particles, and reaction mixture burst out violently from the apparatus; otherwise the polymerisation would have been quantitative in a few minutes. [d] Even sodium allyloxide in allyl alcohol (10 ml.) gave no polymerisation after 2 hr. [e] Using sodium *n*-pentyl oxide catalyst (10 ml.) gave a rather "explosive polymerisation" and part of the polymerisation mixture evaporated; yield 20·5 g. after 5 min. [f] Use of sodium benzyloxide catalyst (10 ml.) gave an "explosive polymerisation."

Preliminary experiments on the specific activating effect of alcohol in the anionic polymerisation of vinyl monomers were carried out. Use of catalyst solutions prepared from sodium alkoxides dissolved in different alcohols of various acidities gave very important results. Small additions of relatively weakly or strongly acidic alcohols, such as phenol, allyl alcohol, butan-1-ol, propan-2-ol and *tert.*-butyl alcohol to methanolic sodium methoxide increased strongly the reactivity of the catalyst (Table 9). For example, the catalyst prepared by addition of propan-2-ol (1 ml.) to methanolic sodium methoxide (3 ml., 5·86N) gave a violently explosive polymerisation after 45 sec. Even weak catalysts such as sodium allyloxide show great reactivity on addition of another alcohol such as methanol. Whereas sodium allyloxide in allyl alcohol gave no polymerisation, its methanolic solution was a strong catalyst (Table 9).

TABLE 9. *Effect of addition of alcohols to methanolic sodium methoxide catalyst.*

Experimental conditions: A solution of methanolic sodium methoxide (3 ml., 5·86N) in various amounts of different alcohols was added in one portion to a cooled mixture of acrylonitrile (40 ml.) and light petroleum (b. p. 40—60°; 75 ml.); reaction temperature −15°.

Added alcohol	Added alcohol (ml.)	Yield (g.)	Time of polymn. (min.)	Induction period (min.)
—	—	2·5	30	—
Allyl	1	8	5	1·5
Allyl	2	explosive	5	4
Phenol	0·5 g.	14	30	2·5
Phenol	1 g.	0	30	—
Butan-1-ol	0·5	7	30	1
Propan-2-ol	1	explosive	—	0·75
Propan-2-ol	2	explosive	—	2·5
tert.-Butyl alcohol	0·5	9	30	1·5

Note: A solution of sodium allyloxide (10 ml., 2·5N) in allyl alcohol was evaporated to dryness *in vacuo* and dissolved in 10 ml. of methanol and added to acrylonitrile (40 ml.) and light petroleum (b. p. 40—60°; 75 ml.) at −15°. After 30 min., 11 g. of polymer were obtained; induction period 17 min.

EXPERIMENTAL

Purification.—Light petroleum (b. p. 40—60°) was dried over sodium and boiled under nitrogen before use. The alcohols were dried over sodium and distilled. Acrylonitrile was dried and distilled to free it from inhibitors. Nitrogen was purified from oxygen by passing it

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through a quartz tube containing fresh copper wire at 600°, then through a solution of 20% of pyrogallol in 20% sodium hydroxide, and dried over concentrated sulphuric acid.

Sodium Alkoxide Catalysts.—These were prepared by dissolving sodium in the respective alcohol under reflux; care was taken to avoid moisture. The alcoholic alkoxide solutions were kept in brown bottles. They must be fresh as they tend to become coloured and decompose. Methanolic sodium methoxide is the most stable. It is difficult to prepare concentrated solutions of the long- or branched-chain alcohols as the solubility of their sodium alkoxides is limited. The concentration of the catalyst solution was determined by titrating an aliquot portion with standard acid with phenolphthalein as indicator.

Polymerisation of Acrylonitrile.—The addition of reagents and the polymerisation were carried out under nitrogen. Into a three-necked flask fitted with a high-speed stirrer and a gas adaptor for introducing nitrogen, the required amounts of acrylonitrile and light petroleum were added. The stirred mixture was cooled (ice–salt bath) to −15° and the temperature kept constant. The catalyst solution was then added from a pipette. The polymerisation started after an induction period and a white solid polymer formed. The polymerisation was stopped after the required time by adding 100 ml. of cooled hydrochloric acid (1 : 1 v/v). The mixture was stirred for 20 min. and then poured into ice-water. The polymer was filtered off, and washed with alcohol and then with water until the filtrate was neutral to litmus and dried to constant weight in an electric oven at 60°. The polymer was obtained as fine white granules because the acrylonitrile was dispersed as fine droplets in the cold light petroleum.

DEPARTMENT OF ORGANIC CHEMISTRY, HEBREW UNIVERSITY,
JERUSALEM, ISRAEL. [*Received, September 12th*, 1958.]

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190. *Studies with Acetylenes. Part III.* The Synthesis of Three partly-*cis*-Diphenyloctatetraenes.*

By M. AKHTAR, T. A. RICHARDS, and B. C. L. WEEDON.

The two 1 : 8-diphenyloctatrienynes and a 1 : 8-diphenyloctadienediyne have been prepared and converted by partial hydrogenation into *cis*-1-, *cis*-3-, and *cis*-3 : *cis*-5-isomers of 1 : 8-diphenyloctatetraene.

DURING the fundamental studies by Zechmeister and his co-workers of the stereochemistry of polyenes [1] it was shown that irradiation of " all-*trans* " 1 : 8-diphenyloctatetraene gives three new geometrical isomers which were designated *cis*-I, *cis*-II, and *cis*-III.[2] These were assigned *cis*-3-, *cis*-1-, and either *cis*-1 : *cis*-3- or *cis*-1 : *cis*-5-structures,† respectively, from a consideration of their light-absorption properties and stabilities. In other investigations we prepared the two monoacetylenic analogues of 1 : 8-diphenyloctatetraene, which we have now used to test some of these stereochemical deductions. Few similar comparisons of synthetic materials and products of stereomutation have been reported previously.[3]

Copper-catalysed condensation [4] of either the Grignard reagent or the lithium derivative of phenylacetylene with 1 : 4-dibromobut-*trans*-2-ene gave crystalline 1 : 8-diphenyloct-4-ene-1 : 7-diyne (I). On reduction this yielded the known 1 : 8-diphenyloctane,[5] and with hot methanolic potassium hydroxide an isomeric hydrocarbon with

* Part II, Nigam and Weedon, *J.*, 1957, 3868.

† In this paper, when the position of a *cis*-structure is cited, it is to be understood that the other ethylenic centres are *trans*.

[1] Zechmeister, *Experientia*, 1954, **10**, 1; *Chem. Rev.*, 1944, **34**, 267.

[2] Zechmeister and Pinckard, *J. Amer. Chem. Soc.*, 1954, **76**, 4144; Lunde and Zechmeister, *Acta Chem. Scand.*, 1954, **8**, 1421; cf. Zechmeister and Le Rosen, *J. Amer. Chem. Soc.*, 1942, **64**, 2755.

[3] Pinckard, Wille, and Zechmeister, *ibid.*, 1948, **70**, 1938; Robeson, Cawley, Weisler, Stern, Eddinger, and Chechak, *ibid.*, 1955, **77**, 4111; Oroshnik, *ibid.*, 1956, **78**, 2651; Gansser and Zechmeister, *Helv. Chim. Acta*, 1957, **40**, 1757.

[4] Danehy, Killian, and Nieuwland, *J. Amer. Chem. Soc.*, 1936, **58**, 611.

[5] Evans and Whalley, *J.*, 1954, 3642.

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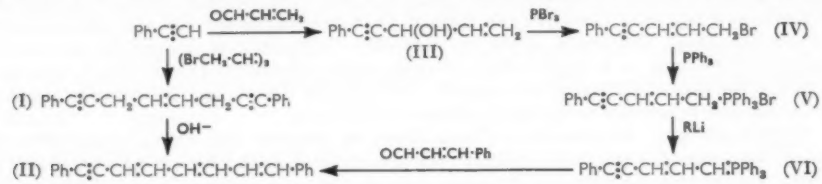
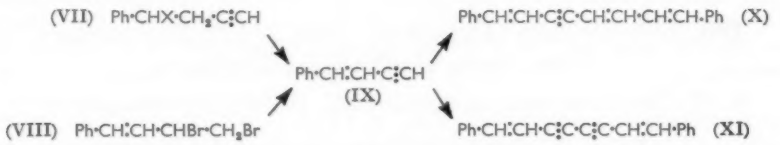
light absorption in good agreement with that expected for a 1 : 8-diphenyloctatrienyne. By analogy with the prototropic rearrangements of other acetylenic compounds (cf. conversion of octa-2 : 6-diynedioic acid into octa-2 : 4-dien-6-ynedioic acid [6]), this product



was formulated as the 1 : 3 : 5-trien-7-yne (II). This structure was confirmed by the following alternative synthesis.

Grignard reaction of phenylacetylene with acraldehyde furnished the alcohol (III) which underwent simultaneous bromination and anionotropic rearrangement on treatment with phosphorus tribromide to give the bromide (IV). This reacted with triphenylphosphine, to give a crystalline phosphonium salt (V) which on dehydrobromination with either butyl- or phenyl-lithium was converted into the corresponding phenylpentenynylidenephosphoran (VI). The last compound with cinnamaldehyde then gave 1 : 8-diphenylocta-1 : 3 : 5-trien-7-yne (II), identical with the product obtained from the diphenyloctenediyne. (1 : 6-Diphenylhexa-1 : 3-dien-5-yne was prepared similarly from the phosphoran and benzaldehyde.)



The alternative 1 : 8-diphenyloctatrienyne was obtained by an extension of Strauss's synthesis of 1 : 4-diphenylbutenyne from phenylacetylene.[7] Styrylacetylene (IX) was prepared by dehydrohalogenation of 4-chloro-[8] (VII; X = Cl) and 4-bromo-4-phenylbut-1-yne [8] (VII; X = Br) and 3 : 4-dibromo-1-phenylbut-1-ene [9] (VIII), the use of sodamide in liquid ammonia giving the best results. Aeration of a solution of the copper salt of styrylacetylene in hot acetic acid then furnished 1 : 8-diphenylocta-1 : 3 : 7-trien-5-yne (X).

Both diphenyloctatrienynes had the same melting point, and a mixture of the two gave a depression of only 2°. Their visible light absorption maxima were at very similar wavelengths (Table 1), but the isomers were readily distinguished by their infrared spectra. Though the routes to the two diphenyloctatrienynes are not stereospecific, there seems little doubt that the homogeneous crystalline products isolated have *trans*-configurations about the three double bonds; this view is confirmed by the infrared data discussed below. The conversion of both materials into " all-*trans* " 1 : 8-diphenyloctatetraenes (see below) establishes their basic carbon skeletons.

Carefully controlled partial reduction of acetylenic analogues over Lindlar catalyst [10] has been used previously in the polyene field to prepare both " hindered " and " unhindered " *cis*-isomers of known configuration.[11] Similar partial reduction of the two diphenyloctatrienynes furnished diphenyloctatetraenes which can therefore be formulated

[6] Jones, Shaw, and Whiting, *J.*, 1954, 3212.
[7] Strauss, *Annalen*, 1905, **342**, 225; cf. Akhtar and Weedon, *Proc. Chem. Soc.*, 1958, **303**.
[8] René-Golse and Le van Thoi, *Compt. rend.*, 1950, **230**, 210.
[9] Rüber, *Ber.*, 1903, **36**, 1404; cf. Muskat and Huggins, *J. Amer. Chem. Soc.*, 1929, **51**, 2496.
[10] Lindlar, *Helv. Chim. Acta*, 1952, **35**, 446.
[11] Inhoffen, Bohlmann, Bartram, Rummert, and Pommer, *Annalen*, 1950, **570**, 54; Isler, Lindlar, Montavon, Rüegg, and Zeller, *Helv. Chim. Acta*, 1956, **39**, 249; Isler, Chopard-dit-Jean, Montavon, Rüegg, and Zeller, *ibid.*, 1957, **40**, 1256.

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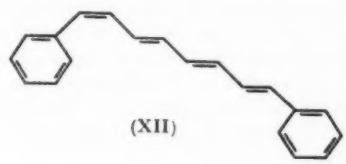
as the *cis*-1- (XII) and *cis*-3-isomers (XIII).* Scale models indicate that a planar conformation of the *cis*-1-isomer is greatly strained owing to steric interference between the hydrogen atom at position 3 and one at an *ortho*-position in the aromatic ring, but that

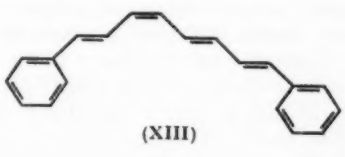
TABLE 1. *Light absorption of diphenyloctatetraenes and their acetylenic analogues* ($\lambda_{max.}$ *in* mμ; $10^{-3}\varepsilon$ *in parentheses*).

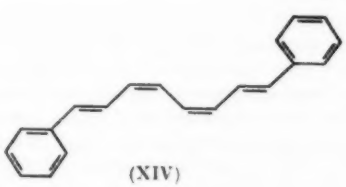
Acetylenes					
7-yne (II) [a]	—	—	—	365 (75)	385 (54)
5-yne (X) [a]	—	—	—	365 (61)	386 (46·5)
3 : 5-diyne (XI) [a]	—	—	335 (40)	360 (43·5)	380 (33)
Tetraenes					
cis-1 (XII) [b]	268 [a]	280	—	368	—
cis-II [b,d]	271	280	—	364	—
cis-3 (XIII) [c]	275 (24·5)	284 (27·5)	355 (59·5)	373 (78)	393 (57)
cis-I [b,d]	273 (23)	283 (28)	352 (57)	369 (78)	391 (56)
cis-3 : *cis*-5 (XIV) [c]	—	—	350 (37)	370 (48)	390 (31)
cis-III [b,d]	—	—	—	359	—
" all-*trans* " (XV) [a]	—	—	355 (71·5)	373 (106)	395 (85)
" all-*trans* " (XV) [b,d]	—	—	352 (74)	371 (108)	393 (85·5)

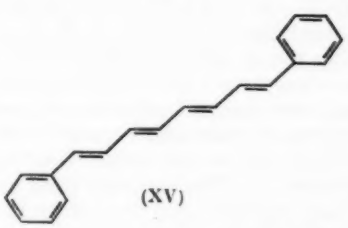
[a] Inflexion. [b] In $CHCl_3$. [c] In hexane. [d] In *cyclo*hexane. [e] Zechmeister and Pinckard.[2]

the *cis*-3 structure is subject to little strain. In agreement, the two *cis*-isomers have markedly different stabilities and light absorptions (Table 1): the *cis*-1-form has a degraded spectrum lacking in fine structure, whereas the *cis*-3-isomer exhibits three intense light-absorption maxima at wavelengths almost identical with those of the " all-*trans* " form (XV), and a well-developed " *cis*-peak; " the *cis*-1-isomer was extremely labile to light and heat; both mono-*cis*-forms on irradiation were converted into mixtures from which


(XII)


(XIII)


(XIV)


(XV)

" all-*trans* " diphenyloctatetraene (XV) was isolated. These properties, and the infrared spectra of the *cis*-1- and *cis*-3-isomer, tally well with those reported by Zechmeister *et al.*[2] for their *cis*-II and *cis*-I isomers respectively, confirming their stereochemical conclusions.

A *cis*-3 : *cis*-5-structure was also considered by Zechmeister and Pinckard [2] for their *cis*-I isomer, but rejected in favour of the unhindered mono-*cis*-configuration. By oxidative coupling of styrylacetylene, and partial reduction of the resulting diacetylene (XI), the *cis*-3 : *cis*-5-isomer (XIV) has now been prepared. Its melting point is higher than that of the other known *cis*-isomers of 1 : 8-diphenyloctatetraene. Its main light-absorption maxima are similar to those of the *cis*-I isomer but are of lower intensity. Moreover, as predicted by Zechmeister and Pinckard, it shows no pronounced " *cis*-peak." On

* See footnote † on p. 933.

irradiation it yields a mixture from which "all-*trans*" diphenyloctatetraene has been isolated.

Some significant features of the infrared spectra of the diphenyloctatetraenes and their acetylenic analogues are summarised in Table 2. Both diphenylocta-*cis*-1- and

TABLE 2. *Infrared light absorption of diphenyloctatetraenes and their acetylenic analogues* ($\lambda_{max.}$ *in* μ *with an indication of intensity; media shown in superscripts*).

	CH in-plane deformation *cis*-CH:CH	CH out-of-plane deformation of *trans*-CH:CH		CH out-of-plane deformation *cis*-CH:CH	CH out-of-plane deformation of Ph groups	
Acetylenes						
7-yne (II)	—[f]	10·07vs	—[f]	—[c]	13·29s[c]	13·42s[c]
5-yne (X)	—[f]	10·21s[f]	10·53s[f]	—[c]	—[c]	13·42vs[c]
3 : 5-diyne (XI)	—[f]	—[f]	10·51vs	—[c]	—[c]	13·41vs[c]
Tetraenes						
cis-1 (XII)	7·08w[a]	10·00s[a]	10·27m[a]	?	?	?
cis-II[b]	7·05m[f]	10·05vs[c]	10·30s[c]	12·95s[c]	—[c]	13·41s[c]
cis-3 (XIII)	7·05m[a]	10·11s[c]	10·31s[c]	12·89ms[c]	—[c]	13·39s[c]
cis-I[b]	7·05m[f]	10·11s[c]	10·30s[c]	12·91ms[c]	—[c]	13·37s[c]
cis-3 : *cis*-5 (XIV)	7·28m[a]	10·15ms[a]	10·55s[a]	12·85m[a]	—[c]	13·54s[a]
cis-III[b]	7·00m[f]	10·10s[c]	10·30s[c]	12·95s[c]	—	13·37s[c]
"all-*trans*" (XV)	—[a]	9·95s, 10·00s[a]	—[a]	—[a]	13·3*[a]	13·45s[a]
"all-*trans*" (XV)[b]	—[g]	9·90vs[g]	—[g]	—[g]	13·27s[g]	—[g]

* Inflexion. [a] In $CHCl_3$. [c] In *cyclo*hexane. [g] In KBr disc. [f] In CCl_4. [g] Mull in mineral oil. [b] Lunde and Zechmeister.[2] w, weak; m, medium; ms, medium strong; s, strong; vs, very strong.

-*cis*-3-tetraene exhibit a band at 7·05—7·08 μ which is absent from the spectrum of the "all-*trans*" isomer, and can be attributed to the in-plane C–H bending vibration of the *cis*-double bonds: this band is absent from the spectra of the two diphenyloctatrienynes and the diphenyloctadienediyne. In the *cis*-3 : *cis*-5-isomer the band is displaced to 7·28 μ, and is thus similar to the 7·31 μ band previously observed with 1 : 4-diphenylbuta-*cis* : *cis*-diene.[2] If such a shift is tentatively assumed to be characteristic of two contiguous *cis*-double bonds, it indicates that Zechmeister's *cis*-III diphenyloctatetraene has the *cis*-1 : *cis*-5- rather than the *cis*-1 : *cis*-3-structure.

The band due to the C–H out-of-plane vibrations of *trans*-carbon–carbon double bonds is split in the *cis*-diphenyloctatetraenes. Lunde and Zechmeister [2] have suggested that the lower-wavelength maximum is associated with any conjugated *trans*-double bond, and the longer-wavelength band with a *trans*-double bond conjugated with a *cis*-double bond. The splitting is particularly pronounced in the *cis*-3 : *cis*-5-isomer. Both compounds, (X) and (XI), with a (*trans*-)double bond conjugated with an acetylenic, but not an ethylenic, linkage have a C–H deformation band at 10·5 μ. The marked differences in the 10·0—10·6 μ range, together with those in the 13·2—13·6 μ region associated with hydrogen out-of-plane rocking in the phenyl groups, enable the two diphenyloctatrienynes to be readily distinguished.

All the *cis*-diphenyloctatetraenes have a band at *ca.* 12·9 μ which is absent from the spectrum of the "all-*trans*" isomer, and may be attributed to C–H out-of-plane rocking in the *cis*-carbon–carbon double bonds. The absence of a band in this region in the spectra of the diphenyloctatrienynes and the diphenyloctadienediynes again shows that these compounds possess *trans*-configurations about their carbon–carbon double bonds.

EXPERIMENTAL

M. p.s were determined on a Kofler block and are corrected. Spectra reported in the Tables above are not repeated in this section.

All operations were carried out in an inert atmosphere. Those involved in the preparation

of the *cis*-diphenyloctatetraenes were performed, so far as possible, in the dark at temperatures not exceeding 20°.

1 : 8-*Diphenyloct*-4-*ene*-1 : 7-*diyne* (I).—(*a*) [*With* H. K. Black]. Cuprous chloride (0·6 g.) was added to a stirred and cooled (ice–salt) suspension of phenylacetylenylmagnesium bromide (prepared from 15·3 g. of phenylacetylene by the method of Black, Horn, and Weedon [12]) in ether (110 c.c.). 1 : 4-Dibromobut-*trans*-2-ene (16·1 g.) in ether (70 c.c.) was added during 40 min. The mixture was stirred at 20° overnight, then under reflux for 3 hr. and finally cooled. Excess of dilute acetic acid was added, and the ethereal layer was separated, washed with water, dried (Na_2SO_4), and evaporated. The residue (9·2 g.) solidified and had m. p. 58—61°. Recrystallisation from light petroleum (b. p. 40—60°) gave **1 : 8-*diphenyloct*-4-*ene*-1 : 7-*diyne*** as long prisms, m. p. 60—61° (Found: C, 93·75, 93·4; H, 6·25, 6·3. $C_{20}H_{16}$ requires C, 93·7; H, 6·3%), $\lambda_{max.}$ (in ethanol) 240 and 251 mμ (ε 37,000 and 38,500 respectively).

(*b*) Phenylacetylene (11·2 g.) in ether (16 c.c.) was added to a solution of phenyl-lithium (from 1·65 g. of lithium) in ether (80 c.c.), and the mixture was heated under reflux for 1½ hr. and then cooled. Cuprous chloride (0·4 g.) was added, followed by a solution of 1 : 4-dibromobut-*trans*-2-ene (10·7 g.) in ether (45 c.c.). The mixture was boiled under reflux for 24 hr., then cooled and poured into 10% v/v acetic acid (200 c.c.). Isolation and crystallisation of the product as in (*a*) gave the hydrocarbon (6·4 g., 54%), m. p. and mixed m. p. 59—61°.

1 : 8-*Diphenyloctane*.—A solution of the above diphenyloctenediyne (2·0 g.) in ethyl acetate (25 c.c.) was shaken with Adams catalyst (58 mg.) in hydrogen until absorption ceased (953 c.c. at 24°/758 mm., equivalent to 5·0 double bonds). Removal of catalyst and solvent, and distillation of the residue, gave 1 : 8-diphenyloctane (1·4 g.), b. p. 137—138°/0·1 mm., n_D^{21} 1·5313. Its infrared absorption was in good agreement with that reported by Evans and Whalley [5] who give b. p. 138—142°/0·1—0·2 mm., n_D^{23} 1·5290.

5-*Phenylpent*-1-*en*-4-*yn*-3-*ol* (III).—Acraldehyde (16·0 g.) in ether (100 c.c.) was added during 30 min. to a stirred suspension of phenylacetylenylmagnesium bromide (prepared from 26 g. of phenylacetylene) in ether (200 c.c.). The mixture was stirred at 20° for 2 hr. and for 30 min. under reflux. It was then cooled, and an excess of saturated aqueous ammonium chloride was added. Isolation of the product with ether, and distillation, gave the ***alcohol*** (21·0 g.), b. p. 100—104°/1 mm., n_D^{23} 1·5740—1·5747, n_D^{31} 1·5710—1·5720 (Found: C, 83·45; H, 6·5. $C_{11}H_{10}O$ requires C, 83·55; H, 6·35%).

1-*Bromo*-5-*phenylpent*-2-*en*-4-*yne* (IV).—Phosphorus tribromide (10·0 g.) in ether (10 c.c.) was added during 30 min. to a stirred and cooled (−8°) solution of the preceding alcohol (19·0 g.) in ether (50 c.c.). The mixture was stirred at 0° for 1 hr., then at 20° for 3 hr. The resulting product was poured on ice and water. Isolation with ether and distillation gave the ***bromide*** (21·0 g.), b. p. 96—100°/1 mm., n_D^{22} 1·6450—1·6465 (Found: C, 59·9; H, 4·4. $C_{11}H_9Br$ requires C, 59·7; H, 4·05%), $\lambda_{max.}$ (in ethanol) 285 mμ (ε 22,000). For the corresponding alcohol Haynes *et al.*[13] report maxima at 259, 272, and 289 mμ (ε 19,000, 26,000 and 21,000 respectively).

Triphenyl*-(5-*phenylpent*-2-*en*-4-*ynyl*)*phosphonium Bromide (V).—The preceding bromide (6·0 g.) was added to a shaken and cooled (−10°) solution of triphenylphosphine (7·4 g.) in benzene (18 c.c.). The mixture was kept at 20° for 48 hr., and the solid (13 g.) which had separated was then collected. Two crystallisations from alcohol gave the ***phosphonium bromide*** as colourless plates, m. p. 192—193° (Found: C, 71·2, 71·15; H, 5·45, 5·6. $C_{29}H_{24}BrP,\frac{1}{2}EtOH$ requires C, 71·15; H, 5·35%), $\lambda_{max.}$ (in ethanol) 268 and 298 mμ (ε 33,500 and 21,000 respectively).

1 : 8-*Diphenylocta*-1 : 3 : 5-*trien*-7-*yne* (II).—(*a*) 1 : 8-Diphenyloct-4-ene-1 : 7-diyne (1·0 g.) was added to a solution of potassium hydroxide (4·0 g.) in methanol (40 c.c.), and the mixture was stirred at 80° for 3 hr. The resulting orange solution was decanted from an insoluble gum and cooled. The crystals which separated (103 mg., 10%) were collected and had m. p. 137—145°. Recrystallisation from *n*-hexane gave **1 : 8-*diphenylocta*-1 : 3 : 5-*trien*-7-*yne*** as yellow plates, m. p. 146—147° (Found: C, 93·6; H, 6·55. $C_{20}H_{16}$ requires C, 93·7; H, 6·3%).

In a small-scale experiment under identical conditions spectral examination of the reaction mixture indicated 54% conversion of the diphenyloctenediyne into fully conjugated isomers.

(*b*) Butyl-lithium (equiv. to 56 mg. of lithium) in ether (8·5 c.c.) was added to a suspension of the triphenyl(phenylpentenynyl)phosphonium bromide (2·7 g.) in ether (30 c.c.), and the

[12] Black, Horn, and Weedon, *J.*, 1954, 1704.
[13] Haynes, Heilbron, Jones, and Sondheimer, *J.*, 1947, 1583.

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mixture was stirred for 1½ hr. at 20°. Cinnamaldehyde (1·1 g.) was then added, and the mixture stirred at 20° for 20 min., then under reflux for 20 min. The mixture was cooled and dilute hydrochloric acid was added. The mixture was filtered and the solid was extracted with ether. The ethereal filtrate and washings were combined, washed with aqueous sodium carbonate, dried (Na_2SO_4), and evaporated. Crystallisation of the residue (1·0 g.) from aqueous alcohol gave yellow needles (150 mg.), m. p. 140—146°. Recrystallisation from the same solvent gave the hydrocarbon, m. p. 146—147·5° undepressed on admixture with a specimen from (*a*). The two samples had the same spectra. Admixture with a specimen of 1 : 8-diphenylocta-1 : 3 : 7-trien-5-yne gave a depression of 2°.

1 : 8-*Diphenylocta*-cis-1 : trans-3 : trans-5 : trans-7-*tetraene* (XII).—A solution of the preceding diphenyloctatrienyne (50 mg.) in ethyl acetate (10 c.c.) containing quinoline (20 mg.) was shaken in the dark with Lindlar catalyst [10] (50 mg.) in hydrogen until 1·1 mol. had been absorbed (4·81 c.c. at N.T.P.). The catalyst was filtered off and the solvent was evaporated under reduced pressure. The residue was triturated with a small volume of methanol, and the solid was separated by centrifugation and removal of the supernatant liquid with a pipette. Two further washings with methanol in the same way gave the crude mono-*cis*-tetraene (*ca.* 21 mg.) which was dissolved in hexane and examined spectrally [max. at 280 and 368 mμ and an inflexion at 268 mμ (*E* 0·109, 0·807, and 0·101 respectively) (Zechmeister and Pinckard report maxima at 271 and 364 mμ and an inflexion at 280 mμ)]. After exposure to light for 2 days the hexane solution exhibited maxima at 262, 353, 371, and 393 mμ (*E* 0·062, 0·815, 1·151, and 1·01 respectively).

The preceding partial hydrogenation was repeated and, after removal of the catalyst, the ethyl acetate solution was kept in sunlight for 24 hr. Evaporation of the solvent, trituration of the residue at 0° with methanol, and filtration then gave a mixture (25 mg.) of geometrical isomers of diphenyloctatetraene. Crystallisation from chloroform gave the "all-*trans*" isomer (9 mg.), m. p. 235—236°, undepressed on admixture with a specimen prepared according to Kuhn and Winterstein's method.[14]

1 : 6-*Diphenylhexa*-1 : 3-*dien*-5-*yne*.—Phenyl-lithium (from 108 mg. of lithium) in ether (30 c.c.) was added to a suspension of the triphenyl(phenylpentenynyl)phosphonium bromide (2·9 g.) in ether (10 c.c.), and the mixture was stirred for 3 hr. Benzaldehyde (1·3 g.) was added and the mixture was stirred at 20° for 2½ hr. and under reflux for 10 min. The mixture was cooled and a solution of concentrated hydrochloric acid (3 c.c.) in water (50 c.c.) was added. Isolation of the crude product (1·0 g.) in the usual way, and crystallisation from aqueous alcohol, gave yellow needles (170 mg.), m. p. 99—100°. Recrystallisation from the same solvent gave the *hydrocarbon*, m. p. 103—104° (Found: C, 93·6, 93·55; H, 6·55, 6·45. $C_{18}H_{14}$ requires C, 93·9; H, 6·1%), $\lambda_{max.}$ (in chloroform) 265 and 340 mμ (ε 4800 and 31,000 respectively).

4-*Chloro*-4-*phenylbut*-1-*yne* (VII; X = Cl).—Reaction of 1-phenylbut-3-yn-1-ol [15] (10·0 g.) in pyridine (5·6 g.) with thionyl chloride (8·0 g.) by the method of René-Golse and Le van Thoi [8] gave the chloride (5·5 g.) as a pale yellow mobile liquid, b. p. 72—84°/1 mm., n_D^{22} 1·5549—1·5560 (lit.,[8] b. p. 75°/2 mm., n_D^{20} 1·5555).

4-*Bromo*-4-*phenylbut*-1-*yne* (VII; X = Br).—Phosphorus tribromide (11·5 g., 15% excess) was added during 20 min. to a cooled (ice) and stirred solution of 1-phenylbut-3-yn-1-ol (15 g.) and pyridine (4 c.c.) in ether (25 c.c.). The mixture was stirred for a further 15 min. at 0° and for 20 min. at 35—40°. A colourless solid which had separated was filtered off and extracted with ether (200 c.c.). The filtrate and extracts were combined, washed with water, saturated sodium carbonate, and again with water, then dried (Na_2SO_4) and evaporated. Distillation of the residue gave the bromide (12 g., 57%) as a pale yellow liquid, b. p. 88—89°/0·5 mm., n_D^{21} 1·5850, which solidified at 0° and after crystallisation from ethanol had m. p. 31° (lit.,[8] b. p. 95°/2 mm., n_D^{20} 1·5747), and $\lambda_{max.}$ (in alcohol) 223 mμ (ε 6300).

3 : 4-*Dibromo*-1-*phenylbut*-1-*ene* (VIII).—1-Phenylbuta-1 : 4-diene [16] was treated with bromine according to Riiber's directions.[9] The dibromide had m. p. 94—95° (Riiber [9] gives m. p. 94°).

1-*Phenylbut*-1-*en*-3-*yne* (*Styrylacetylene*) (IX).—(*a*) Dehydrochlorination of 4-chloro-4-phenylbut-1-yne (5·7 g.) with potassium hydroxide (5·0 g.) in ethanol (40 c.c.) by the method of René-Golse and Le van Thoi [8] gave 1-phenylbut-1-en-3-yne as a very unstable liquid, b. p.

[14] Kuhn and Winterstein, *Helv. Chim. Acta*, 1928, **11**, 87.
[15] Henbest, Jones, and Walls, *J.*, 1949, 2696.
[16] Braude, Jones, and Stern, *J.*, 1947, 1087.

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56—60°/5 mm., n_D^{21} 1·6068 (lit.,[8] b. p. 59°/2 mm., n_D^{20} 1·6123). The yields in successive experiments were 30, 50, and 40%. The product readily gave a copper salt with ammoniacal cuprous chloride.

(*b*) 4-Chloro-4-phenylbut-1-yne (7·8) was added in 5 min. to a stirred solution of sodamide (prepared [17] from 3·5 g. of sodium) in liquid ammonia (150 c.c.), and the mixture was stirred for 4 hr. Ammonium chloride (12 g.) was added cautiously, and the ammonia was allowed to evaporate overnight. Water (200 c.c.) was added to the residue, and the product was extracted with ether (150 c.c.). The extract was washed with water, dried (Na_2SO_4), and evaporated. Distillation of the residue gave the hydrocarbon (3·0 g., 55%), b. p. 56°/1 mm., n_D^{24} 1·6095.

(*c*) Treatment of 4-bromo-4-phenylbut-1-yne (11·8 g.) with sodamide (from 3·5 g. of sodium) in liquid ammonia (200 c.c.), and isolation of the product in the same way, gave the hydrocarbon (5·7 g., 80%), b. p. 46°/5 mm., n_D^{22} 1·6120, $\lambda_{max.}$ (in ethanol) 220, 227, and 278 mμ (ε 15,500, 11,000, and 30,500 respectively). The mercury salt crystallised from benzene and had m. p. 163°.

(*d*) A solution of 3 : 4-dibromo-1-phenylbut-1-ene (32 g.) in ether (150 c.c.) was added slowly to a solution of sodamide (from 8·0 g. of sodium) in liquid ammonia (400 c.c.), and the mixture was stirred for 3 hr. Addition of ammonium chloride (20 g.), and isolation of the product as described under (*b*), gave the hydrocarbon (4·4 g., 30%), b. p. 58—59°/2 mm., n_D^{21} 1·6157.

Copper Styrylacetylide.—Cuprous chloride (8·0 g.) was added to freshly prepared, saturated aqueous ammonium carbonate (400 c.c.). To the resulting suspension dilute aqueous ammonia was added cautiously until a clear blue solution was obtained. To this was added 1-phenylbut-1-en-3-yne (3·0 g.) in ethanol (25 c.c.), and the mixture was stirred vigorously for 30 min. The yellow precipitate was collected, washed successively with dilute ammonia, water, ethanol, and ether, and dried in a vacuum-desiccator, to give the copper acetylide (3·9 g.) as an orange powder.

The different batches of 1-phenylbut-1-en-3-yne reported above all gave the copper acetylide in 80—90% yield.

1 : 8-*Diphenylocta*-1 : 3 : 7-*trien*-5-*yne* (X).—Finely divided copper styrylacetylide (1·5 g.) was added to acetic acid (60 c.c.) in a 250 c.c. two-necked flask fitted with an efficient reflux condenser. The mixture was boiled and, when the suspended copper salt had been converted into a flocculent brown precipitate (5—10 min.), air was aspirated through the mixture at a rate which was just sufficient to cause appreciable loss of solvent through the condenser. After the mixture had developed a greenish colour (40—50 min.), a few drops were withdrawn every 2 min., diluted with water, and extracted with ether. When no insoluble copper salt was visible at the water–ether interface in the test sample, the reaction was interrupted, and the deep green mixture was cooled, diluted with water (2 vol.), and extracted with ether. The extracts were washed with aqueous sodium carbonate until free from acetic acid, then with water, dried (Na_2SO_4), and evaporated. Repeated recrystallisation of the residue (0·4 g., 40%), m. p. 135—147°, from ethanol gave 1 : 8-*diphenylocta*-1 : 3 : 7-*trien*-5-*yne* (0·2 g.) as pale yellow plates, m. p. 146—147° (Found: C, 93·55; H, 6·4. $C_{20}H_{16}$ requires C, 93·7; H, 6·3%).

Continuation of the æration after the stage indicated above resulted in a very impure product.

1 : 8-*Diphenylocta*-trans-1 : cis-3 : trans-5 : trans-7-*tetraene* (XIII).—A solution of the preceding diphenyloctatrienyne (53·0 mg.) in ethyl acetate (5 c.c.) was shaken with Lindlar catalyst [10] (50 mg.) in the dark in an atmosphere of hydrogen. After 4 hr., when 1·1 mol. of hydrogen had been absorbed (5·23 c.c. at N.T.P.), the reaction was interrupted and the catalyst and solvent were removed. Crystallisation of the residue from ether–light petroleum (b. p. 40—60°) gave the mono-*cis*-tetraene (32 mg.) as yellow needles, m. p. 135—136° (Found: C, 93·15; H, 7·05. Calc. for $C_{20}H_{18}$: C, 92·95; H, 7·05%). The same m. p. was observed when determined in an evacuated capillary tube (Zechmeister and Pinckard [2] give m. p. 139—141°).

When the molten tetraene was heated at 160—170° it resolidified and afterwards remelted at 227—230°.

Irradiation of a solution of the mono-*cis*-tetraene (1·6 mg.) and a trace of iodine (0·027 mg.) in *cyclo*hexane (50 c.c.) with a " photoflood " lamp for 15 min. gave a mixture of stereoisomers, $\lambda_{max.}$ 275, 285, 355, 375, and 395 mμ (ε 6000, 6000, 69,000, 98,000, and 77,000).

A solution of the mono-*cis*-tetraene (10 mg.) in benzene (15 c.c.) and hexane (50 c.c.) was kept before an ultraviolet lamp for 15 min. and then evaporated. Crystallisation of the residue from chloroform gave " all-*trans* " 1 : 8-diphenyloctatetraene (4 mg.), m. p. and mixed m. p. 232—234°.

[17] Vaughn, Vogt, and Nieuwland, *J. Amer. Chem. Soc.*, 1934, **56**, 2120.

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1 : 8-*Diphenylocta*-1 : 7-*diene*-3 : 5-*diyne* (XI).—(*a*) Finely divided copper styrylacetylide (2·0 g.) was added to a solution of potassium ferricyanide (8·0 g.) in water (70 c.c.), and the suspension was stirred vigorously for 3 hr. at 60—80°. The resulting thick brown suspension was extracted repeatedly with ether. The extracts were combined, washed with water, dried (Na_2SO_4), and evaporated. Crystallisation of the residue from chloroform–light petroleum (b. p. 40—60°) gave the *diphenyloctadienediyne* (0·17 g.) as pale yellow needles, m. p. 133—134° (Found: C, 94·25; H, 5·8. $C_{20}H_{14}$ requires C, 94·5; H, 5·5%).

(*b*) Finely divided copper styrylacetylide (1·3 g.) was added to a solution of ammonium chloride (12·0 g.) and cuprous chloride (8·0 g.) in water (50 c.c.) and 9N-hydrochloric acid (1 c.c.). The suspension was shaken in oxygen for 6 hr. during which 800 c.c. of oxygen were absorbed. Dilute hydrochloric acid was added to decompose a greenish complex which had separated, and a yellow precipitate was then filtered off. By extraction with ether the yellow solid was separated into an insoluble residue of unchanged copper styrylacetylide (0·3 g.) and the required hydrocarbon (0·2 g.), m. p. and mixed m. p. 133—134°.

(*c*) Freshly prepared 1-phenylbut-1-en-3-yne (2·0 g.) in alcohol (30 c.c.) was added to a solution of cuprous ammonium chloride (from 16·2 g. of ammonium chloride and 10·3 g. of cuprous chloride) in water (200 c.c.) which had been acidified to pH 4—5 by the addition of concentrated hydrochloric acid (3 drops). The mixture was shaken in oxygen until absorption ceased (600 c.c.; 6 hr.). Dilute hydrochloric acid was added to dissolve a light green precipitate, which had formed during the reaction, and a yellow solid was filtered off, dried, and extracted with ether. Evaporation of the extract and crystallisation of the residue from chloroform–light petroleum (b. p. 40—60°) yielded the required hydrocarbon (1·25 g., 60%), m. p. and mixed m. p. 133—133·5°.

1 : 8-*Diphenylocta*-trans-1 : cis-3 : cis-5 : trans-7-*tetraene* (XIV).—A solution of the preceding diphenyloctadienediyne (52·2 mg.) in ethyl acetate (5 c.c.) was shaken with Lindlar catalyst (50 mg.) in the dark in an atmosphere of hydrogen until 2·1 mol. of gas had been absorbed (8—12 hr. in different experiments). Removal of catalyst and solvent at 20° and crystallisation of the residue at −40° in the dark from ether–light petroleum gave the *di*-cis-*tetraene* (16 mg.) as yellow plates, m. p. 191—193° (Found: C, 92·5; H, 6·95. $C_{20}H_{18}$ requires C, 92·95; H, 7·05%).

When the molten tetraene was heated it resolidified and afterwards remelted at 222—226°.

Irradiation of a solution of the di-*cis*-tetraene (1·6 mg.) and a trace of iodine (0·027 mg.) in *cyclo*hexane (50 c.c.) with an ultraviolet lamp for 15 min. gave a mixture of stereoisomers, $\lambda_{max.}$ 275, 285, 355, 375, and 395 mμ (ε 6500, 6500, 65,000, 98,000, and 79,000 respectively).

A solution of the di-*cis*-tetraene (7 mg.) in benzene (15 c.c.) and hexane (50 c.c.) was kept before an ultraviolet lamp for 15 min. and then evaporated. Crystallisation of the residue from chloroform gave " all-*trans* " 1 : 8-diphenyloctatetraene (4 mg.), m. p. and mixed m. p. 234—235·5°.

Microanalyses and spectral measurement were carried out in the microanalytical (Miss J. Cuckney) and spectrographic laboratories (Mrs. A. I. Boston, Mr. R. L. Erskine) of this Department. One of the authors (M. A.) thanks the Pakistan Government for a research grant, and another (T. A. R.) thanks Imperial Chemical Industries Limited, Dyestuffs Division, for study leave.

Department of Chemistry, Imperial College of Science and Technology,
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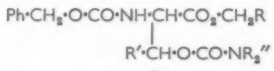
191. *Cyto-active Amino-acids and Peptides. Part VII.*[1] *Derivatives of Serine and Threonine.*

By F. Bergel and Roy Wade.

Amino-acid derivatives carrying the " nitrogen-mustard " radical as an amido-group have been synthesised in the form of *O*-[*NN*-di-(2-chloroethyl)-carbamoyl]-DL- and -L-serine and -DL-threonine. A number of other *N*-substituted *O*-carbamoylserines have been prepared. The *N*-benzyloxycarbonyl- and *N*-*p*-nitrobenzyloxycarbonyl-threonine, and to a smaller extent the corresponding serine compounds, produced oxazolidones on treatment with alkali.

In view of the contrasting biological behaviour of the serine and threonine " mustards," the hydrolysis of these two compounds *in vitro* was studied and *iso*propyl *NN*-di-(2-chloroethyl)carbamate was synthesised. This compound, like the threonine derivative, was inactive in anti-tumour tests while the serine and the ethyl carbamate " mustards " showed remarkable activity.

Previous papers in this series[2] and the work of Larionov and Knunyants and their co-workers[3,4] have dealt with the synthesis of α-amino-acid derivatives containing a " nitrogen-mustard " substituent (M) on an aromatic nucleus. Other amino-acid derivatives, carrying M on the α-carbon atom in place of an unsubstituted amino-group, have been described by Ishidate and his co-workers[5] and more recently by Nyhan and Busch.[6] The work of Skinner *et al.*[7,8] showing *O*-carbamoylserine and *O*-(hydrazinocarbonyl)serine to be antagonists of glutamine in various bacterial systems indicates that corresponding derivatives of serine carrying M in the carbamoyl moiety might possess antitumour activity.



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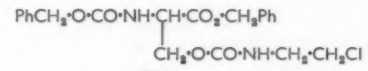

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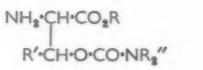

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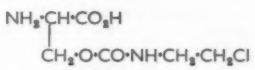

(IV)

This paper describes the preparation of several derivatives of serine and threonine in which a $-CO-$ group is used to provide the link between the α-amino-β-hydroxy-acid and amido-groups with potential cytotoxicity. *N*-Benzyloxycarbonyl-DL- and -L-serine benzyl ester and -DL-serine methyl ester were prepared by slight modification of known methods[7,9-13] and converted into the *O*-chlorocarbonyl derivatives by reaction with carbonyl chloride. These were not characterised but coupled directly in an inert solvent with di-(2-chloroethyl)amine, dipropylamine, or 2-chloroethylamine, a second equivalent of base being used to take up the hydrogen chloride formed in the reaction. The coupling

[1] Parts V and VI, Bergel and Stock, *J.*, 1959, 90, 97.
[2] Part I, Bergel and Stock, *J.*, 1954, 2409; Part II, Bergel, Burnop, and Stock, *J.*, 1955, 1223; Part III, Bergel and Lewis, *J.*, 1957, 1816; Part IV, Bergel and Stock, *J.*, 1957, 4563.
[3] Larionov, Shkodinskaja, Troosheikina, Khoklor, Varina, and Novikova, *Lancet*, 1955, II, 169.
[4] Knunyants, Kil'disheva, and Golubeva, *Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk*, 1956, 1418.
[5] Ishidate, Sakurai, and Izumi, *J. Amer. Pharm. Assoc.*, 1955, **44**, 132.
[6] Nyhan and Busch, *Fed. Proc.*, 1958, **17**, 639.
[7] Skinner, McCord, Ravel, and Shive, *J. Amer. Chem. Soc.*, 1956, **78**, 2412.
[8] McCord, Ravel, Skinner, and Shive, *ibid.*, 1958, **80**, 3762.
[9] Bergmann and Zervas, *Ber.*, 1932, **65**, 1192.
[10] Ben-Ishai and Berger, *J. Org. Chem.*, 1952, **17**, 1564.
[11] Baer and Maurukas, *J. Biol. Chem.*, 1955, **212**, 25.
[12] Jones and Lipkin, *J. Amer. Chem. Soc.*, 1956, **78**, 2408.
[13] Fölsch and Mellander, *Acta Chem. Scand.*, 1957, **11**, 1232.

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of di-(2-chloroethyl)amine with ethyl chloroformate in a similar manner has been described by Childs *et al.*[14] The resulting carbamoyl derivatives (I and II; R′ = H; Table 1, Nos. 1—5) were in general low-melting solids with physical properties similar to those of the starting material. The protecting benzyloxycarbonyl and benzyl ester groups were removed by hydrogenolysis in methanol in presence of palladium–charcoal; uptake of hydrogen was usually rapid and the free amino-acid derivatives and one ester hydrochloride (III; R′ = H; and IV) are described in Table 2.

In the case of the threonine derivatives, *N*-benzyloxycarbonyl-DL-threonine was prepared by the reaction of the amino-acid with benzyloxycarbonyl chloride in aqueous sodium hydrogen carbonate, as carried out by Riley, Turnbull, and Wilson.[15] After use of a stronger alkali as in the conventional Bergmann technique[9] there was no precipitation of the product on acidification; however, extraction of the clear aqueous solution with ethyl acetate and working up the extract gave about 50% yield of a compound which was readily water-soluble, giving a strongly acid solution with a negative ninhydrin test and

TABLE 1.

	Compound (I)				Yield		Found (%)				Required (%)			
No.	R	R′	R″	M. p.	(%)	Formula	C	H	N	Cl	C	H	N	Cl
1	Ph	H	Cl·CH_2·CH_2	70—71° [b]	71	$C_{22}H_{25}O_6N_2Cl_3$	55·55	5·5	5·6	14·3	55·5	5·2	5·6	14·3
2 [a]	Ph	H	,,	54—55 [c]	83	$C_{22}H_{26}O_6N_2Cl_3$	56·3	5·2	5·6	14·1	55·5	5·2	5·6	14·3
3		Compound (II)		102—103 [d]	75	$C_{21}H_{23}O_6N_2Cl$	58·4	5·5	6·4	7·9	58·1	5·3	6·45	8·2
4	Ph	H	Pr[n]	56—57 [c]	82	$C_{23}H_{28}O_6N_2$	65·8	7·2	6·2	—	65·8	7·0	6·1	—
5	H	H	Cl·CH_2·CH_2	79—80 [b]	63	$C_{17}H_{22}O_6N_2Cl_2$	48·2	5·3	6·7	17·0	48·5	5·2	6·7	16·9
6	Ph	Me	,,	80—81 [c]	65	$C_{24}H_{28}O_6N_2Cl_2$	56·8	5·4	5·3	14·0	56·4	5·5	5·5	13·9

[a] L-Isomer of No. 1, $[\alpha]_D^{23}$ −13·5° (*c* 1 in EtOH). [b] From ethyl acetate–light petroleum (b. p. 60—80°). [c] From ether–light petroleum (b. p. 40—60°). [d] From ethanol.

TABLE 2.

	Compound (III)					
No.	R	R′	R″	M. p.*	Yield (%)	R_F
1	H	H	Cl·CH_2·CH_2	140°	82	0·53
2 [a]	H	H	,,	127	89	0·53
3		Compound (IV)		180	72	0·43
4	H	H	Pr[n]	121	85	0·71
5 [b]	Me	H	Cl·CH_2·CH_2	115—116	95	0·78
6	H	Me	,,	130	95	0·60

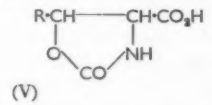
		Found (%)				Required (%)			
No.	Formula	C	H	N	Cl	C	H	N	Cl
1	$C_8H_{14}O_4N_2Cl_2$	35·0	5·3	10·3	25·4	35·2	5·1	10·3	26·0
2 [a]	$C_8H_{14}O_4N_2Cl_2,H_2O$	33·2	5·7	9·6	24·4	33·0	5·5	9·6	24·4
3	$C_8H_{11}O_4N_2Cl$	34·6	5·4	13·1	16·8	34·3	5·2	13·3	16·9
4	$C_{16}H_{20}O_4N_2$	52·0	8·9	12·5	—	51·7	8·7	12·1	—
5 [b]	$C_9H_{17}O_4N_2Cl_3$	33·3	5·1	8·7	32·7	33·4	5·4	8·7	32·9
6	$C_9H_{16}O_4N_2Cl_2,H_2O$	35·7	6·1	9·1	22·9	35·4	5·9	9·2	23·3

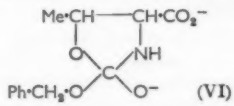
* With decomp. [a] L-Isomer, $[\alpha]_D^{22}$ +6·0° (*c* 1 in H_2O), $[\alpha]_D^{23}$ +22·0° (*c* 1 in N-HCl). [b] Isolated as the hydrochloride. [c] Run on Whatman No. 1 paper, ascending-descending technique with butan-1-ol–ethanol–propionic acid–water (10 : 5 : 2 : 5 v/v).

analyses as for $C_5H_7O_4N$. Hydrolysis in concentrated acid solution gave DL-threonine once again, identified by its *N*-benzoyl derivative. The compound is probably 5-methyl-2-oxo-oxazolidine-4-carboxylic acid (V; R = Me) in which the asymmetric carbon atoms have the same configuration as in DL-threonine. Such a cyclisation may well involve the transient formation of the intermediate (VI) followed by elimination of benzyl alcohol. An intermediate of this nature has been suggested previously[16] in cases of $N \longrightarrow O$ acyl migration which was obviously not observed under our alkaline conditions. Gish and

[14] Childs, Goldsworthy, Harding, King, Nineham, Norris, Plant, Selton, and Tompsett, *J.*, 1948, 2174.
[15] Riley, Turnbull, and Wilson, *J.*, 1957, 1373.
[16] Welsh, *J. Amer. Chem. Soc.*, 1949, **71**, 3500.

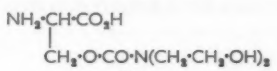
Carpenter,[17] in their work on the *p*-nitrobenzyloxycarbonyl derivatives of α-amino-acids, noticed that the yields were low with the serine and threonine derivatives when strongly alkaline conditions were used. They reported that these derivatives were rapidly hydrolysed by strong alkali with liberation of *p*-nitrobenzyl alcohol. While these authors [17] did not isolate any product from the amino-acid portion, we found that oxazolidones were

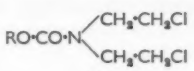

(V)


(VI)

indeed formed from *N*-*p*-nitrobenzyloxycarbonyl-DL-threonine (yield 60%) and in much smaller quantities from the corresponding *N*-benzyloxycarbonyl- and *N*-*p*-nitrobenzyloxycarbonyl-serine in addition to the threonine derivative mentioned above.

The last compound, which was not obtained crystalline, was converted into the benzyl ester by the procedure adopted for the analogous serine compound. Treatment of this ester with carbonyl chloride, as before, followed by coupling with di-(2-chloroethyl)amine gave a product which consisted mainly of starting material. Fractionating the mother-liquors on alumina gave only a small yield of chlorine-containing material which was recrystallised and gave the correct analysis for *N*-benzyloxycarbonyl-*O*-[*N*-di-(2-chloroethyl)carbamoyl]-DL-threonine benzyl ester. The preparation was subsequently repeated, the carbonyl chloride being allowed to remain in contact with benzyloxycarbonyl-DL-threonine benzyl ester for a total time of 14 days by introducing more of the chloride to the solution from time to time. From this a better yield of carbamoyl derivative was obtained. When the initial preparation, using carbonyl chloride treatment for 4 hours, was repeated in the presence of one equivalent of dimethylaniline, formation of the chlorocarbonyl derivative was more rapid and this gave finally a 65% yield of the required carbamoyl derivative (I; R = Ph, R′ = Me, R″ = CH_2·CH_2Cl; Table 1, No. 6). The compound was hydrogenolysed in the usual way and the free amino-acid derivative (III; R = H, R′ = Me, R″ = CH_2·CH_2Cl; Table 2, No. 6) was obtained in good yield.

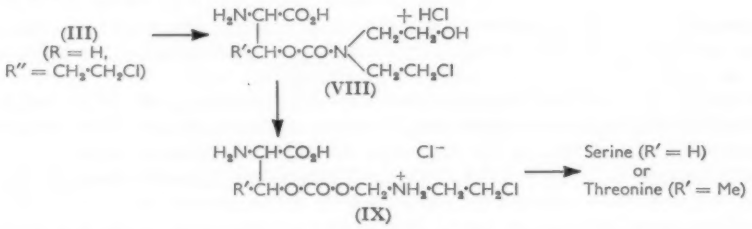

(VII)


(X)

The DL- and L-serine mustards (Table 2, No. 1, CB 3159, and No. 2, CB 3189), compounds of low toxicity, were found to be very effective (the L more so than the DL) as anti-tumour agents against the Walker rat carcinoma 256. CB 3159 was also tested on the very resistant benzopyrene and "August" tumours in rats and caused some hold-up of their growth rates, but the methyl ester hydrochloride (Table 2, No. 5, CB 3178) showed a greater effect on the latter tumour, but no effect on the transplanted mammary tumour in C^- male mice. Both the other serine derivatives examined (Table 2, Nos. 3 and 4) proved to be inactive on the Walker carcinoma, as did the threonine mustard (Table 2, No. 6, CB 3182). This prompted us to compare the hydrolytic behaviour of the serine derivative CB 3159 and the threonine derivative CB 3182: it was found that under *in vitro* conditions, at pH 7·4 and 37°, CB 3182 produced acidity at roughly twice the rate of CB 3159. When the two amino-acids were treated at 100° in aqueous solution (starting pH 5·7) and hydrolysis was followed chromatographically on paper, more rapid breakdown of the threonine derivative was again observed. In addition to this overall rate difference the pathway of degradation of the serine derivative went *via* two ninhydrin-positive, relatively stable intermediates before any free serine was produced. On the other hand, during the hydrolysis of CB 3182, free threonine appeared at an earlier stage, although an analogous sequence of degradation products was observed, implying a greater lability

[17] Gish and Carpenter, *J. Amer. Chem. Soc.*, 1953, **75**, 950.

of the second intermediate. The chemical constitution of each intermediate has not been determined yet with certainty although the possibility that either of them is the dihydroxy-analogue (VII) is ruled out by their different R_F values when chromatographed on paper in phenol. By analogy with the behaviour of di-(2-chloroethyl)amides of carboxylic acids which undergo $N \longrightarrow O$ acyl migration under acid conditions [14] the annexed scheme is tentatively postulated.



The quantitative differences in the hydrolysis of CB 3159 and CB 3182 are seemingly too small to account for the marked difference in biological activity of the two compounds; moreover the evidence so far available, albeit under *in vitro* conditions, does not allow for the formation of di-(2-chloroethyl)amine. The situation is probably different *in vivo*, where enzymic reactions may liberate the cytotoxically active di-(2-chloroethyl)amine or in some other way remove the deactivating influence of the acyl group on the chlorine atoms of the " nitrogen mustard."

The problem is somewhat reminiscent of that obtaining with urethane derivatives (X). As mentioned above, Childs *et al.*[14] have reported the synthesis of the urethane (X; R = Et). Dr. S. R. M. Bushby [15] has tested this and various homologues for anti-tumour activity against the Walker carcinoma. He found it was active but that replacement of the ethyl by other alkyl radicals diminished considerably, or completely eliminated, this activity. We prepared the compound (X; R = Pr^i) because of its broad analogy with the serine–threonine relationship, and like the threonine mustard (CB 3182) this urethane was inactive.

Experimental

*Benzyloxycarbonyl-*DL*-serine Benzyl Ester.*—Benzyloxycarbonyl-DL-serine was prepared by the method of Bergmann and Zervas [9] in 83% yield. Esterification by Ben-Ishai and Berger's general procedure [10] gave a crude product which was heated to 100—120°/1 mm. for 30 min. to remove excess of benzyl alcohol. The residual gum crystallised from ether on addition of light petroleum, as needles, m. p. 73—74° (lit.,[7,11–13] 72—73° to 74·0—74·4°).

*Benzyloxycarbonyl-*L*-serine Benzyl Ester.*—The protected ester, prepared in the same way as above, crystallised from ether as needles, m. p. 82—83° (lit.,[11–13] 83—84° to 84—85°), $[\alpha]_D^{21}$ −8·8° (*c* 5·0 in EtOH) [lit.,[12] −8·7° (*c* 5 in EtOH)].

N-*Benzyloxycarbonyl-O-chlorocarbonyl-*DL*- and -*L*-serine Benzyl Ester.*—Essentially the general procedure as described by Skinner *et al.*[7] was used. Carbonyl chloride was passed into a stirred suspension of benzyloxycarbonyl-DL- or -L-serine benzyl ester (10 g.) in benzene or toluene (200 ml.) at 0° for 20 min. The gas inflow and cooling were then stopped but the stirring was continued for 3 hr. A stream of dry nitrogen was bubbled through the by then clear solution until all the hydrogen chloride and excess of carbonyl chloride had been removed and the solvent was evaporated off under reduced pressure at <40°. No attempt was made to crystallise the residual oil which was used directly in the coupling experiments.

Substituted N-*Benzyloxycarbonyl-O-carbamoyl-*DL*- and -*L*-serine Benzyl Ester* (I and II).—Solutions of the chloroformate, prepared as above in benzene (about 3 ml./g.), were stirred and cooled during slow addition of solutions of various bases (2·3 equivs.) in ether (about 5 ml./g.). The solutions were kept at room temperature overnight then washed with dilute acid, sodium hydrogen carbonate solution, and water, dried (Na_2SO_4), and evaporated to

[15] Bushby, personal communication.

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dryness under reduced pressure at $\gtrsim 35°$. The *carbamates* crystallised from the solvents indicated in Table 1 (Nos. 1—4).

DL-*Serine Methyl Ester Hydrochloride.*—The ester prepared by Fischer and Suzuki's method [19] had m. p. 134° (decomp.). These authors give m. p. 114° (decomp.), as do Mattocks and Hartung,[20] but King [21] gives m. p. 134° (decomp.).

N-*Benzyloxycarbonyl*-DL-*serine Methyl Ester.*—The preparation was carried out by a method analogous to that used by Riley, Turnbull, and Wilson [15] for the corresponding ethyl ester. N-*Benzyloxycarbonyl*-DL-*serine methyl ester* had b. p. 178—183°/1 mm. (Found: C, 57·1; H, 6·1; N, 5·5. $C_{12}H_{15}O_5N$ requires C, 56·9; H, 6·0; N, 5·5%).

N-*Benzyloxycarbonyl*-O-[NN-*di*-(2-*chloroethyl*)*carbamoyl*]-DL-*serine Methyl Ester.*—*N*-Benzyloxycarbonyl-DL-serine methyl ester (7·0 g.) was converted into the *O*-chlorocarbonyl derivative in the same way as the benzyl ester described above. This was then coupled in benzene (40 ml.) with di-(2-chloroethyl)amine (9·5 g., 2 equivs.) and after being worked up in the usual way the *carbamate* recrystallised as recorded in Table 1 (No. 5).

N-*Benzyloxycarbonyl*-DL-*threonine Benzyl Ester.*—*N*-Benzyloxycarbonyl-DL-threonine was prepared from DL-threonine (10 g.) by the method of Riley *et al.*[15] but was not obtained crystalline and was converted (18·9 g.) into the benzyl ester directly, by boiling benzyl alcohol (18 ml.), benzene (180 ml.), and toluene-*p*-sulphonic acid (0·5 g.), with a Dean and Stark water-separator. After 8 hr. the esterification was complete and the cooled solution was washed with sodium hydrogen carbonate solution and with water and dried (Na_2SO_4). The benzene was evaporated off on the water-pump and the excess of benzyl alcohol on the oil-pump (bath-temp. 100—120°). Trituration of the residual oil with light petroleum caused crystallisation, and recrystallisation of the solid from ether–light petroleum gave N-*benzyloxycarbonyl*-DL-*threonine benzyl ester* as needles, m. p. 63—64° (13·65 g., 49% based on threonine) (Found: C, 66·3; H, 6·1; N, 4·2. $C_{19}H_{21}O_5N$ requires C, 66·5; H, 6·2; N, 4·1%).

Attempted Preparation of Benzyloxycarbonyl-DL-*threonine in Aqueous Alkali.*—As in Bergmann and Zervas's method,[9] DL-threonine (2·4 g.) was dissolved in 4N-sodium hydroxide (5 ml.), the solution cooled (<5°), and benzyl chloroformate (3·8 ml.) added portionwise with vigorous shaking. Between each addition 2N-sodium hydroxide was added to maintain pH 8—10. After all the chloroformate had been added, the mixture was shaken for 1 hr., then extracted with ethyl acetate (2 × 20 ml.). Careful addition of concentrated hydrochloric acid gave neither a precipitate nor a turbidity, in contrast to the preparation mentioned above.[15] Extraction with ethyl acetate (4 × 25 ml.) was followed by drying (Na_2SO_4); evaporation of the solvent under reduced pressure gave a solid residue which recrystallised from ethyl acetate–light petroleum as prisms (1·5 g., 52%), m. p. 123—124°, of *5-methyl-2-oxo-oxazolidine-4-carboxylic acid* (Found: C, 41·6; H, 4·9; N, 9·6. $C_5H_7O_4N$ requires C, 41·4; H, 4·9; N, 9·6%).

Treatment of N-*Benzyloxycarbonyl*-DL-*threonine and* -DL-*serine and* N-p-*Nitrobenzyloxycarbonyl*-DL-*threonine and* -DL-*serine with Alkali.*—The acids (0·01 mol.) were dissolved in 2N-sodium hydroxide (10 ml., 2 equiv.) with shaking at room temperature. After a few minutes each solution became turbid and an oil was formed which in the case of the *p*-nitro-derivatives rapidly crystallised. Extraction with ethyl acetate (3 × 10 ml.) removed the benzyl or *p*-nitrobenzyl alcohol, and the aqueous layer was acidified by the dropwise addition of concentrated hydrochloric acid. The clear aqueous solution was extracted with ethyl acetate (6 × 15 ml.), and the organic layer dried (Na_2SO_4) and evaporated to dryness. Trituration with light petroleum caused the residues to crystallise, and the solids recrystallised from ethyl acetate–light petroleum. The two threonine derivatives gave DL-5-methyl-2-oxo-oxazolidine-4-carboxylic acid, m. p. and mixed m. p. 123—124°. The two serine derivatives gave DL-2-*oxo-oxazolidine-4-carboxylic acid*, m. p. 125—126° (Found: C, 36·2; H, 3·9; N, 10·7. $C_4H_5O_4N$ requires C, 36·6; H, 3·8; N, 10·7%).

Acid-hydrolysis of 5-Methyl-2-oxo-oxazolidine-4-carboxylic Acid.—The acid (500 mg.) was boiled with concentrated hydrochloric acid (10 ml.) for 6 hr. After evaporation to dryness the residue was dissolved in ethanol (5 ml.), and morpholine (0·5 ml.) was added. White crystals separated and were filtered off, washed with a little ethanol, and recrystallised from aqueous ethanol. This gave 350 mg. of threonine, m. p. 236° (decomp.).

The amino-acid was benzoylated (Schotten–Baumann) and the *N*-benzoyl derivative

[19] Fischer and Suzuki, *Ber.*, 1905, **38**, 4193.
[20] Mattocks and Hartung, *J. Biol. Chem.*, 1946, **165**, 501.
[21] King, *J. Amer. Chem. Soc.*, 1947, **69**, 2738.

recrystallised from ethyl acetate–light petroleum to give rods, m. p. and mixed m. p. 144—145° with *N*-benzoyl-DL-threonine.

N-Benzyloxycarbonyl-O-[NN-di-(2-chloroethyl)carbamoyl]-DL-threonine Benzyl Ester.—*N*-Benzyloxycarbonyl-DL-threonine benzyl ester (6·8 g.) was dissolved in dry benzene (70 ml.), dimethylaniline (2·53 ml., 1 equiv.) added, and carbonyl chloride passed through the stirred solution at 5° for 20 min. Stirring was continued for a further 4 hr. at room temperature. Next day dry nitrogen was used to remove excess of carbonyl chloride, and the dimethylaniline hydrochloride removed by washing the solution with dilute acid. The organic layer was dried (Na_2SO_4) and treated with ethereal di-(2-chloroethyl)amine (6·2 g., 2·2 equiv.) in the usual way. Solid material began to separate almost immediately but stirring was continued for 3 hr. After working up, the required *carbamate* was obtained in 65% yield (see Table 1, No. 6).

An attempted preparation by the method successfully applied to the serine derivative (see above) gave only a 3% yield. This was separated from unchanged starting material by passing a benzene solution down an alumina column. The carbamate passed straight through whereas the hydroxy-compound was retarded somewhat.

Repetition of this preparation but with the carbonyl chloride and the hydroxy-compound in contact for 2 weeks gave a 37% yield.

Substituted O-Carbamoyl-DL- and -L-serine and -DL-threonine Derivatives.—The fully protected carbamate derivatives were dissolved in methanol (8—10 g. per 200 ml.) and hydrogenolysed with 5% palladium–charcoal (200 mg.). Uptake of hydrogen was complete in a few hours, the catalyst was filtered off, and the solvent removed under reduced pressure at $\not>40°$. In the case of *N*-benzyloxycarbonyl-*O*-[*N*-di-(2-chloroethyl)carbamoyl]-DL-serine methyl ester, concentrated hydrochloric acid (2 ml.) was added to the methanolic solution before hydrogenolysis and the product isolated as the *hydrochloride*. The products are recorded in Table 2.

O-[*N*-Di-(2-chloroethyl)carbamoyl]-DL-serine methyl ester hydrochloride was also prepared by saturating a suspension of the corresponding amino-acid (Table 2, No. 1) in dry methanol (1 g. per 15 ml.) with hydrogen chloride at 5°. The resulting clear solution was evaporated to dryness and the residue recrystallised from methanol–ether (yield 78%).

Hydrolysis Experiments on O-[NN-*Di-(2-chloroethyl)carbamoyl*]-DL-*serine* (CB 3159) *and on* O-[NN-*Di-(2-chloroethyl)carbamoyl*]-DL-*threonine* (CB 3182).—The compound (0·1 mmol.) was dissolved in water (50 ml.) contained in a jacketed vessel fitted with a magnetic stirrer and kept at 37°. Atmospheric carbon dioxide was precluded by releasing a slow stream of argon near the surface. A Pye automatic titrator was used to regulate the addition of 0·01N-sodium hydroxide to adjust the solution to pH 7·4 and maintain this value for 24 hr.

Volumes of 0·01N-alkali required to maintain pH 7·4 for 24 hr. were: CB 3159, 2·75 ml.; CB 3182, 5·35 ml.

TABLE 3. *Aqueous hydrolyses.*

	CB 3159; R_F				CB 3182; R_F			
Time	0·05	0·08	0·10	0·53	0·08	0·11	0·15	0·60
Zero	—	—	—	++++	—	—	—	++++
5 min.	—	+	—	+++	+	+	—	++
15 min.	+	++	—	+	+	++	+	—
30 min.	+	++	—	—	+	++	+	—
45 min.	+	++	+	—	+	+	++	—
1 hr.	+	++	+	—	+	+	++	—
2 hr.	++	+	++	—	+	—	++	—
3 hr.	++	+	++	—	+	—	++	—
5 hr.	+	+	++	—	+	—	+++	—
6 hr.	+	—	+++	—	—	—	++++	—
Amino-acid standard	—	—	++++	—	—	—	++++	—

The relative intensities of the spots are shown by the number of + signs, *e.g.*, ++++ = very strong, etc.

We are indebted to Dr. W. Davis for carrying out these determinations.

In the experiments at 100°, the " mustards " (25 mg.) were boiled in water (5 ml.). Samples (0·01 ml.) were withdrawn from time to time, spotted on paper (W-1), and chromatographed with butanol–ethanol–propionic acid–water (10 : 5 : 2 : 5) as solvent. After 18 hours' running the chromatogram was developed with ninhydrin (0·25% in acetone); the ninhydrin-positive spots are shown in Table 3.

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These may be interpreted as showing that, in the case of CB 3159, the "mustard" (R_F 0·53) is decomposed into a first relatively stable intermediate (R_F 0·08) which itself is decomposed to a second intermediate (R_F 0·05) which breaks down to serine (R_F 0·10). Similarly, the threonine "mustard" (R_F 0·60) gives a first intermediate (R_F 0·11), then a second (R_F 0·08), and finally threonine (R_F 0·15).

With phenol (water-saturated) as solvent, serine and the two preceding intermediates have R_F 0·30, and the di-(2-hydroxyethyl)carbamoyl-DL-serine has R_F 0·72.

iso*Propyl* NN-*Di*-(2-*chloroethyl*)*carbamate*.—*iso*Propyl chloroformate [22] (12·3 g.) in benzene (40 ml.) was added dropwise to a stirred solution of di-(2-chloroethyl)amine, prepared from the hydrochloride (36 g.), in ether (200 ml.), the temperature being kept at 20—25°. Next morning the solution was washed with dilute acid, aqueous sodium hydrogen carbonate solution, and water, and dried (Na_2SO_4), the solvent evaporated, and the residual iso*propyl* NN-*di*-(2-*chloroethyl*)*carbamate* (17·0 g., 65%) distilled under reduced pressure (b. p. 121—123°/1 mm.) (Found: C, 42·3; H, 6·5; N, 5·7; Cl, 31·0. $C_8H_{15}O_2NCl_2$ requires C, 42·1; H, 6·6; N, 6·1; Cl, 31·1%).

We thank Professor A. Haddow and Drs. D. W. Adamson and S. R. M. Bushby for permission to mention the biological results. We are very grateful to Mr. W. Hopwood for his valuable technical assistance. The analyses were carried out by the Microanalytical Laboratory, Organic Chemical Department, Imperial College of Science and Technology, and Mr. P. R. W. Baker, Beckenham. This investigation has been supported by grants to this Institute from the British Empire Cancer Campaign, the Jane Coffin Childs Memorial Fund for Medical Research, the Anna Fuller Fund, and the National Cancer Institute of the National Institutes of Health, U.S. Public Health Service.

CHESTER BEATTY RESEARCH INSTITUTE,
INSTITUTE OF CANCER RESEARCH: ROYAL CANCER HOSPITAL,
FULHAM ROAD, LONDON, S.W.3. [*Received, October 10th*, 1958.]

[22] Thiele and Dent, *Annalen*, 1898, **302**, 269.

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192. *Unstable Intermediates. Part IV.* Electron Spin Resonance Studies of Univalent Aromatic Hydrocarbon Ions.*

By A. CARRINGTON, F. DRAVNIEKS, and M. C. R. SYMONS.

The electron spin resonance spectra of the positive and negative ions of anthracene, naphthacene, and perylene have been analysed and the hyperfine splitting constants obtained. Some aspects of the chemistry of the positive ions are discussed.

MANY workers have observed electron spin resonance absorption from solutions of aromatic hydrocarbons in sulphuric acid. These have usually been attributed to hydrocarbon positive ions although in no case has it been proved that the electron spin resonance spectrum arises exclusively from one paramagnetic entity. Indeed, Yokozawa and Miyashita [1] suggest that the spectrum they obtain from a solution of perylene in concentrated sulphuric acid arises in part from appreciable population of the perylene triplet state and in part from the presence of a separate free radical. The most convincing evidence in favour of the positive ion postulate was obtained by Weissman, de Boer, and Conradi [2] who showed that the spectra obtained from the sulphuric acid solutions were very similar in their general appearance to those obtained from the well-authenticated hydrocarbon negative ions, and that this was in accord with molecular-orbital theory.

The published electron spin resonance spectra of both positive and negative ions are not too well resolved and only for the naphthalene negative ion [3] was it possible to analyse

* Part III, *J.*, 1959, 277.

[1] Yokozawa and Miyashita, *J. Chem. Phys.*, 1956, **25**, 796.
[2] Weissman, de Boer, and Conradi, *ibid.*, 1956, **26**, 963.
[3] Tuttle, Ward, and Weissman, *ibid.*, 1956, **25**, 189.

the spectrum completely and obtain values of the splitting constants for the non-equivalent protons contributing to the hyperfine structure. The demonstration that the splitting due to a proton attached to an aromatic carbon atom is, to a good approximation, proportional to the unpaired electron density at that carbon atom [4] led to the appreciation that the electron spin resonance method should provide a powerful tool for the investigation of electron distributions. This potentiality has not yet been fully realised because few complex hyperfine patterns have been completely and successfully analysed.

We have almost completely resolved the hyperfine structure in the spectra obtained from the positive and negative ions of anthracene, naphthacene, and perylene. This has enabled us to assign precise values to the splitting constants and to show that, for sulphuric acid solutions, the spectra can be interpreted unambiguously in terms of a single paramagnetic species.

Experimental

The electron resonance experiments were made with a spectrometer employing a reflection cavity operating in the TE 0116 mode at 9200 Mc./sec. A magnetic field of approximately 3300 gauss was provided by a magnetically shimmed 6 inch magnet with a battery power supply. The field was modulated at 100 kc./sec. by using one turn of wire around the sample inside the cavity. The signal was amplified at 100 kc./sec., fed through a phase-sensitive detector and recorded on a Sanborn Dual Channel Recorder as the first derivative of the absorption with respect to magnetic field, against the magnetic field. The chart paper was calibrated in gauss by the proton resonance technique and g-values were measured with respect to the diphenylpicrylhydrazyl free radical. The splitting constants in Table 1 are believed to be accurate to $\pm 0{\cdot}05$ gauss and the g-values are accurate to the fourth decimal place, a value of 2·0039 for diphenylpicrylhydrazyl being used.

The positive ions were prepared by dissolving the hydrocarbon in 98% sulphuric acid, the concentrations being 0·01M—0·02M although the line widths were not very dependent upon the concentration. The spectrum of the anthracene positive ion persisted for about 1 hr., but with naphthacene and perylene good spectra were obtained for several weeks after preparation. In no case was any change in symmetry or relative line intensities observed and we can conclude with certainty that only one free radical was formed in each system.

The negative ions were prepared by vacuum distillation of tetrahydrofuran from phosphoric oxide into a tube containing the hydrocarbon and a small piece of potassium. The tubes were sealed off, warmed to melt the potassium, and examined in the spectrometer. The line width in all cases depended very strongly on the hydrocarbon concentration, as has been discussed by Ward and Weissman.[5] With anthracene an interesting sequence was observed. As the potassium dissolved, the radical concentration increased and a spectrum of 21 broad lines was observed. However, the line width decreased with time and after several days we obtained the spectrum shown in Fig. 1. We suggest that the initial line width is due to electron exchange between the radical ion and unchanged anthracene but that exchange between the radical ion and the products must be slow. The sample containing the perylene negative ion still gave a strong well-resolved spectrum after two months.

The hydrocarbons were all recrystallised from ethanol and their m. p.s checked.

Results

The spectra obtained are shown in Figs. 1, 2, and 3, the spectra for the two ions of any one hydrocarbon being shown under identical sweep conditions. The spectra were analysed and the reconstruction shown under each spectrum was computed once the splitting constants for protons occupying different symmetry sites had been determined. The latter are determined largely by trial and error, but once the correct constants have been obtained the agreement between the computed and experimental spectra should be perfect with respect to both relative line intensity and position. Ease of such an analysis depends on the resolution.

The splitting constants are listed in Table 1; positions α, β, and γ are defined in structures (I)—(IV). We have included our values for the naphthalene negative ion since we have been

[4] McConnell, *J. Chem. Phys.*, 1956, **24**, 632.
[5] Ward and Weissman, *J. Amer. Chem. Soc.*, 1954, **76**, 3612.

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FIG. 1. *Electron spin resonance absorption spectra of the anthracene positive and negative ions.*

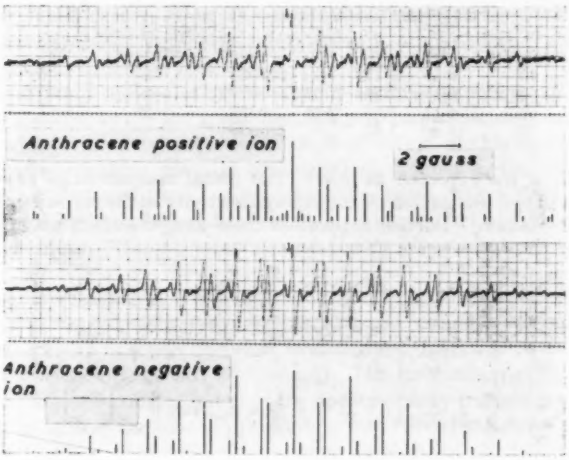


FIG. 2. *Electron spin resonance absorption spectra of the naphthacene positive and negative ions.*

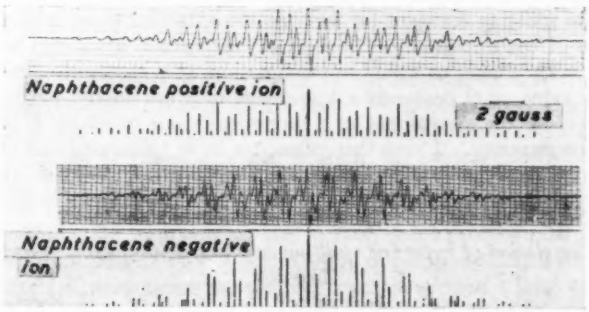


FIG. 3. *Electron spin resonance absorption spectra of the perylene negative and positive ions.*

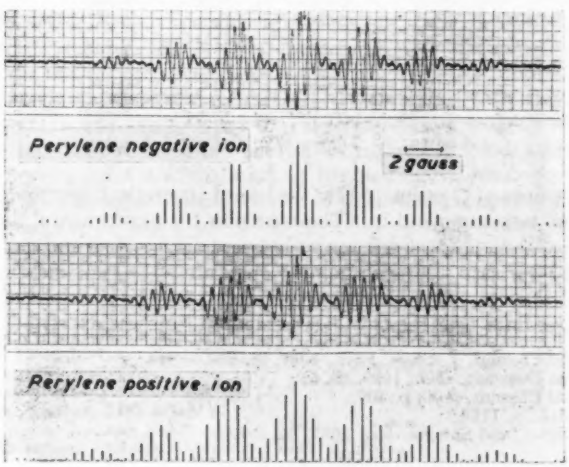
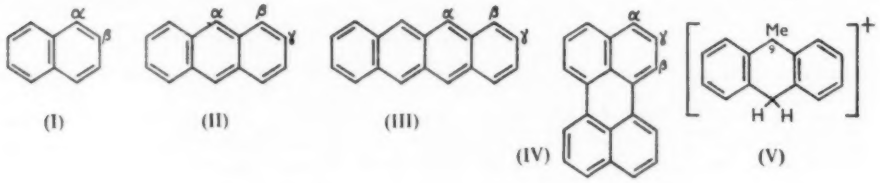


TABLE 1. *Values of the hyperfine splitting constants (in gauss).*

Hydrocarbon	Positive ions: No. of lines observed	a_α	a_β	a_γ	g-value	Negative ions: No. of lines observed	a_α	a_β	a_γ	g-value
Anthracene ...	45	6·65	3·11	1·40	2·0028	41	5·56	2·74	1·57	2·0029
Naphthacene ...	63	5·17	1·74	1·03	2·0028	57	4·25	1·49	1·17	2·0029
Perylene	59	4·11	3·09	0·46	2·0028	59	3·53	3·09	0·46	2·0029
Naphthalene ...	25	4·90	1·83	—	2·0029					

able to resolve all of the expected 25 lines. The initial assignment of the constants to the particular protons shown was guided by the known reactivity of the corresponding ring positions in the parent hydrocarbon. Further support of these assignments is presented below.



(I) (II) (III) (IV) (V)

DISCUSSION

McConnell and his co-workers [6-9] have found that the relationship between the experimental hyperfine splitting constant (a) for a proton attached to an aromatic carbon atom and the density of the unpaired electron (ρ) at that carbon atom can be represented by the equation $a = Q\rho$ where, to a first approximation, Q is constant. In the general case derivation of a value of Q demands a knowledge of ρ but in the particular case of the benzene negative ion the assignment of a numerical value of 23 for Q is independent of any arbitrary assumptions. Using this value, we have calculated the unpaired electron densities from the experimental hyperfine splitting constants and in Table 2 these are compared with the electron densities calculated [10] from Hückel's molecular-orbital theory.

TABLE 2. *Correlation of hyperfine splitting constants with calculated unpaired electron densities.*

		Positive ions: ρ (calc.)	ρ (obs.)	"Q"	Negative ions: ρ (calc.)	ρ (obs.)	"Q"
Anthracene	α	0·192	0·289	34·6	0·192	0·242	28·9
	β	0·096	0·135	32·4	0·096	0·119	28·5
	γ	0·047	0·061	29·8	0·047	0·068	33·4
Naphthacene	α	0·148	0·225	34·9	0·148	0·185	28·7
	β	0·056	0·076	31·1	0·056	0·065	26·6
	γ	0·034	0·045	30·3	0·034	0·051	34·4
Perylene	α	0·108	0·179	38·1	0·108	0·153	32·7
	β	0·083	0·134	37·2	0·083	0·134	37·2
	γ	0·013	0·020	35·3	0·013	0·020	35·3

We also include values of Q estimated by the use of theoretical electron densities but this procedure has less to recommend it. The trends in the experimental data are worthy of comment. There are significant differences between the positive and negative ions which, as Weissman, de Boer, and Conradi [2] pointed out, cannot be explained in terms of simple molecular-orbital theory. The differences are largest for the positions of highest electron density. Also, one finds that the Q values calculated from the experimental data increase

[6] McConnell and Chesnut, *J. Chem. Phys.*, 1957, **27**, 984.
[7] McConnell and Dearman, *ibid.*, 1958, **28**, 51.
[8] McConnell and Chesnut, *ibid.*, p. 107.
[9] McConnell, *ibid.*, p. 1188.
[10] Fukui, Yonezawa, and Shingu, *ibid.*, 1952, **20**, 722.

with increasing size of the hydrocarbon. Without carefully defining what we mean by the electron density at a carbon atom, these values of Q have little significance. Despite the approximations involved, the simple relationship is of great value and in many cases supports the predictions of simple molecular-orbital theory. Hoijtink [11] has recently considered the application of molecular-orbital theory to these problems and concludes that the simple theory is suited to the interpretation of the electron spin resonance spectra of the hydrocarbon mononegative ions since the basic assumption of this theoretical approach, *i.e.*, that the unpaired electron may be considered as moving in the field of the carbon atoms, is not too far removed from reality. In other cases, where the unpaired electron in a neutral alternant hydrocarbon radical forms an integral part of the system, the simple theory is not satisfactory. Simple valence-bond theory gives a better description of such systems.[12]

Chemistry of the Positive Ions.—When an aromatic hydrocarbon is dissolved in concentrated sulphuric acid, three reactions are well established, namely, protonation, oxidation, and sulphonation. There is much chemical evidence for oxidation to form positive ions, much of which has been summarised by Weiss.[13] The mechanism of this oxidation is of interest. Kon and Blois [14] pointed out that the ability of a hydrocarbon to form a positive ion in sulphuric acid follows the ease of protonation (atom localisation energies) rather than the ionisation potentials. This can be understood in terms of the following sequence for anthracene (A):

$$A + H_2SO_4 \rightleftharpoons AH^+ + HSO_4^- \quad (1)\ \text{(rapid)}$$

$$A + AH^+ \rightleftharpoons {\cdot}AH + A^+ \quad (2)$$

$${\cdot}AH + 2H_2SO_4 \rightleftharpoons A^+ + 2H_2O + SO_2 + HSO_4^- \quad (3)$$

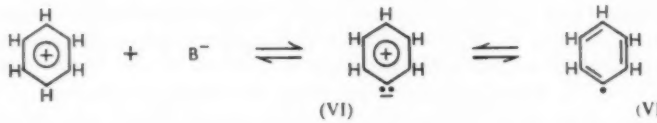
The radical ·AH will be a powerful hydride-ion or hydrogen-atom donor, and stage (3) is simply one of several possible subsequent reactions. It is noteworthy that in oxygen-free HF, which cannot accept hydride ions or hydrogen atoms, only protonation can be detected.

In the specific case of anthracene in acid solution, the evidence for protonation is very strong. Gold and Tye [15] have pointed out the formal similarity between the diphenylmethyl carbonium ion (Ph_2HC^+) and anthracene protonated in the 9-position. Their ultraviolet and visible absorption spectra are, in fact, remarkably similar, the long-wavelength bands having maxima at 4400 Å and 4300 Å respectively. If 9-methylanthracene is dissolved in sulphuric acid under protonating conditions, then a long wavelength band at 4130 Å is found.[16] The methyl group has effected a shift of 170 Å to shorter wavelengths. Protonated 9-methylanthracene (V) bears the same relationship to protonated 1 : 1-diphenylethylene as protonated anthracene (AH^+) bears to the diphenylmethyl carbonium ion. In fact the methyldiphenylmethyl carbonium ion has a peak at 4240 Å, the shift to shorter wavelengths being 160 Å, almost identical with the expected value. These considerations make the assumed structures seem highly plausible, and absence of electron spin resonance absorption from these solutions is also in accord with these postulates.

It is probably correct to assume that the positive ions are entirely separate from the anion HSO_4^-. Concentrated sulphuric acid is an extremely good ionising solvent and electron spin resonance gives no indication of ion pairing. This is equally true of the negative ions in ether solutions. Here, because of the lower dielectric constant, one might expect to find some ion pairing even in dilute solutions, but evidently this cannot be construed as involving covalent bonding since Adam and Weissman's [17] recent results on salts of the type $Ph_2CO^-Na^+$ show strikingly that if the ions are adjacent some charge transfer occurs and the hyperfine structure due to sodium is resolved.

[11] Houtink, *Mol. Phys.*, 1958, **1**, 157.
[12] Brovetto and Ferroni, *Nuovo Cim.*, 1957, **5**, 142.
[13] Weiss, *Nature*, 1941, **147**, 512.
[14] Kon and Blois, *J. Chem. Phys.*, 1958, **28**, 743.
[15] Gold and Tye, *J.*, 1952, 2173 *et seq.*
[16] Grace and Symons, *J.*, 1959, 958.
[17] Adam and Weissman, *J. Amer. Chem. Soc.*, 1958, **80**, 1518.

It is interesting to consider the corresponding conjugate acids and bases of the hydrocarbon ions. In a sufficiently basic medium, hydrocarbon positive ions could lose ring protons. For ease of presentation the benzene positive ion is depicted.



(VI) (VII)

Structure (VI) is converted into (VII) by electron transfer from the sp^2 hybridised lone pair to the ring. When phenyl radicals react they do so invariably as if they had structure (VII), so one can infer that (VII) is a closer representation of the ground state than (VI). However, if phenyl-type radicals were formed in strongly acidic media, protonation should occur, with a consequent decrease in free-radical reactivity.

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UNIVERSITY OF MINNESOTA, MINNEAPOLIS 14, MINNESOTA, U.S.A.
THE UNIVERSITY, SOUTHAMPTON (*present address*, A. C. *and* M. C. R. S.).

[*Received, August 11th*, 1958.]

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193. *Unstable Intermediates. Part V.*[1] *Ozonides and Superoxides.*

By A. D. MCLACHLAN, M. C. R. SYMONS, AND M. G. TOWNSEND.

The preparation and properties of salts containing the ozonide ion, O_3^-, are described. In particular spectrophotometric and magnetic studies have been made which give structural information, and enable a distinction to be made between ozonides and superoxide ions. The transient formation of ozonide ions during the thermal decomposition of potassium hydroperoxide in concentrated aqueous potassium hydroxide and the photochemical decomposition of hydroperoxide ions in an alkali glass have been established.

WHEN ozone is passed over powdered sodium or potassium hydroxide an orange solid ozonide is formed [2] which is remarkably stable. Recent studies [3,4] have indicated that this compound contains the ion O_3^-, which is paramagnetic, containing nineteen valence electrons.

Whilst the radicals OH, O^-, HO_2 and O_2^- are frequently postulated as transient intermediates in a variety of reactions (see, *e.g.*, refs. 5 and 6), the rôle of O_3^- as an intermediate has not been explored, and little attempt has been made to obtain direct physical evidence for the presence of any of these intermediates.

In Parts I, II, and IV we suggested that ultraviolet and electron spin resonance spectroscopy in combination are a powerful and sensitive method for detecting traces of unstable

[1] Parts I—IV, Symons and Townsend, *J.*, 1959, 263; Gibson, Symons, and Townsend, *J.*, 1959, 269; Symons, *J.*, 1959, 277; Carrington, Dravnieks, and Symons, preceding paper.
[2] Wurtz, " Dictionnaire de Chimie pure et appliquée," Vol. II, p. 721, 1868.
[3] Kazarnovskii, Nikolskii, and Abletsova, *Doklady Akad. Nauk, S.S.S.R.*, 1949, **64**, 69.
[4] Whaley and Kleinberg, *J. Amer. Chem. Soc.*, 1951, **73**, 79.
[5] Uri, *Chem. Rev.*, 1952, **50**, 375.
[6] Symons, *J.*, 1953, 3956.

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intermediates, so we have tried to use them in this study. The ultraviolet spectra of solutions of the superoxides in ammonia have been recorded [7] and the electron spin resonance spectrum has been described and interpreted.[8]

The conjugate acids of these ions are less stable and their identification depends far more on inference.[9,10] We therefore decided that in attempts to find reactions in which unstable intermediates of this sort might be formed, attention would be given to basic media.

Hydrogen peroxide decomposes readily in alkaline solution, though the mechanism is uncertain. The decomposition has been studied [11,12] at pH 9—13 but not in more concentrated alkali. Because of its simplicity we chose this reaction. When certain mixtures of aqueous sodium and potassium hydroxide are cooled clear glasses are formed, suitable for spectrophotometry; accordingly, dilute solutions of hydrogen peroxide in such low-temperature glasses were exposed to ultraviolet light, again in the hope that a sufficient build-up in radical concentration would occur to make identification possible.

Experimental and Results

Preparation of Ozonides.—Slow passage of dry ozonised oxygen over finely powdered sodium or potassium hydroxide at room temperature rapidly gave the corresponding ozonides as deep yellow powders. Dissolution of potassium ozonide in liquid ammonia gave a stable orange solution: the sodium salt was insoluble. The solids were stable for many hours in stoppered tubes and could be kept indefinitely at −78°. Attempts to prepare ozonides from lithium hydroxide and alkaline-earth metal hydroxides were unsuccessful.

Preparation of Superoxides.—Sodium superoxide is present as an impurity (*ca.* 10%) in "AnalaR" sodium peroxide.[8] Potassium superoxide, also contaminated with large quantities of the peroxide, was prepared by direct oxidation of potassium. The metal was distilled *in vacuo* (10^{-4} mm.) up a tube (40 cm. long) by means of a small electric furnace in several stages, and was deposited as a thin mirror on the walls of the reaction vessel. The side arm was removed at a constriction, and a small quantity of dried oxygen admitted. On slight warming of one section of the film, vigorous reaction occurred to give a deep yellow powder. This process was repeated until all the metal had been oxidised.

Spectrophotometry.—Spectra were measured with a Unicam S.P. 500 spectrophotometer. Diffuse reflectance measurements were made directly on the powdered solid by use of a Unicam attachment with lithium fluoride as a reference surface. The ozonides are not hygroscopic and the readings were reproducible under ordinary operating conditions.

Spectra of solutions of potassium ozonide in liquid ammonia were measured in 1 cm. stoppered quartz cells in a thermostatted cell holder. Coolant was circulated from a Townson and Mercer low-temperature thermostat by a small pump *via* lagged tubing. The temperature of the cells was estimated to be about −50°. Cold dry nitrogen was circulated through the cell housing to prevent misting of the cell surfaces. The cells were filled with solvent and solution with a pre-cooled dropping pipette, and were cooled in acetone at −78° before being placed in the housing. Thus atmospheric moisture was kept out.

Concentrations of ozonide solutions were estimated by comparing the areas under their electron spin resonance spectra, measured at 90° K, with the areas under similar spectra obtained from calibrated carbon specimens measured under identical conditions. Hence extinction coefficients for solutions in liquid ammonia were estimated. The results are given in Table 1 together with relevant details of the spectra of superoxides.[8] A typical spectrum is shown in Fig. 1.

[7] Thompson and Kleinberg, *J. Amer. Chem. Soc.*, 1951, **73**, 1243.
[8] Bennett, Ingram, Symons, George, and Griffith, *Phil. Mag.*, 1955, **46**, 443; for the method of detection see Ingram, "Spectroscopy at Radio and Microwave Frequencies," Butterworths, London, 1955.
[9] Livingstone, Ghormley, and Zeldes, *J. Chem. Phys.*, 1956, **24**, 483.
[10] Gibson, Symons, and Townsend, *J.*, 1959, 269.
[11] Nicoll and Smith, *Ind. Eng. Chem.*, 1955, **47**, 2548.
[12] Erdey, *Acta. Chim. Acad. Sci. Hung.*, 1953, **3**, 95.

Spectra of irradiated glasses were measured at about 100° K in a Unicam S.P. 500 instrument fitted with a special cell holder.[15] Cells were filled and manipulated as in earlier experiments.[16] The results are given in Table 1 and a typical spectrum is shown in Fig. 2.

TABLE 1. *Details of spectra of superoxide and ozonide ions.*

$\varepsilon_{max.}$ is the molar extinction coefficient at the peak ($\lambda_{max.}$).

Compound	$\lambda_{max.}$ (mμ)	$\varepsilon_{max.}$	Remarks
$NaO_2 + Na_2O_2$	370	—	Diffuse reflectance (shoulder)
O_3^- in NH_3	380	—	Ref. 7
$NaO_3 + NaOH$	440	—	Diffuse reflectance
O_3^- in NH_3	435	2000	Solution
Irradiated HO_3^-	430	—	Irradiated in glass

Magnetic Measurements.—Initial measurements were made at wavelengths of 3 cm., 1·25 cm., and 8 mm., by use of standard " crystal–video " detection.[8,13] Later measurements were made at 3 cm. with phase-sensitive detection,[14] The results reported for the superoxides [8]

FIG. 1. *Spectrum of solid sodium ozonide measured by diffuse reflectance methods.*

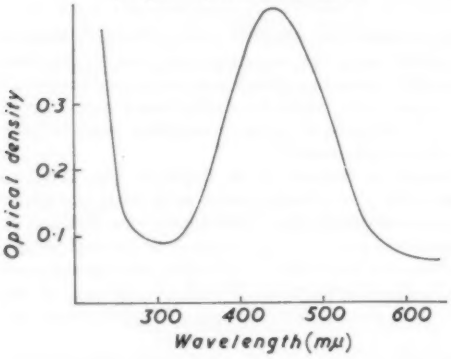
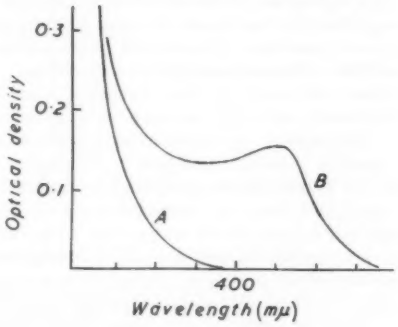


FIG. 2. *Spectrum of a glass composed of sodium and potassium hydroxides, water, and hydrogen peroxide, recorded at* 100° K, (*A*) *before irradiation,* (*B*) *after irradiation with* 3650 Å *light.*



have been confirmed, but the initial results mentioned by Bennett *et al.*[13] for solid ozonides have not. The present results show that under all conditions of measurement a single symmetrical line centred on a *g*-value of 2·012 ± 0·001 and having a total width at half-height of 25 ± 2 gauss is obtained. The curve reported earlier [13] is asymmetric having a shoulder on the high-field side with a *g*-value of about 2·003. This shoulder, close to the free-spin value, was probably caused by a small amount of impurity since no sign of any broadening in this region has been observed in the present study. Whilst it is true that such asymmetry would not be so well resolved at 3 cm. as at 1·25 cm., this is offset by the fact that a relatively narrow line is obtained, and the method of detection whereby the first derivative of the absorption line is recorded, is very sensitive to changes in line shape. The fact that small traces of diphenylpicrylhydrazyl added to the specimen can be clearly detected supports this contention. The results are given in Table 2 and Fig. 3.

Hydrogen Peroxide–Alkali System.—All reagents were carefully purified because it seemed probable that radical formation was induced by traces of impurities (see Discussion). Judactan " Batch tested " potassium hydroxide was dissolved in specially purified water [17] in Polythene vessels. Stock solutions were further purified at times by shaking with alumina and centrifuging. Hydrogen peroxide was 90% triply distilled material kindly supplied by Laporte Chemicals Ltd. Reaction mixtures were prepared in Polythene vessels and rapidly transferred to small

[13] Bennett, Ingram, and Schonland, *Proc. Phys. Soc.*, 1956, **69**, *A*, 556.
[14] Gibson, Ingram, Symons, and Townsend, *Trans. Faraday Soc.*, 1957, **53**, 914.
[15] Symons and Townsend, *Spectrovision*, 1957, **4**, 5.
[16] Symons and Townsend, *J.*, 1959, 263.
[17] Smith and Symons, *Trans. Faraday Soc.*, 1958, **54**, 338.

silica tubes immediately before being frozen in liquid oxygen to quench the reaction. Subsequent measurements of electron spin resonance spectra were made at 90° K. Detectable signals were obtained only when the concentration of potassium hydroxide approached 8M and decayed rapidly at room temperature, a typical half-life being 2 min. Under these conditions a rapid

TABLE 2. *Details of electron spin resonance spectra of superoxide and ozonide ions at* 3 *cm.*

	g-value	Δ_{HH} (gauss) *	Δ_{MS} (gauss) †
NaO_3 (+Na_2O_2)	2·000 ± 0·005 ($g_\perp$)	250	—
	2·175 ± 0·005 ($g_\parallel$)		
NaO_3 (+NaOH)	2·012 ± 0·002	25	20
O_3^- in NH_3	2·012 ± 0·002	24	18
H_2O_2 in KOH (40%)	2·012 ± 0·003	25	19
Irradiated glass (2 min.)	2·012 ± 0·003	25	19
Irradiated glass (6 hr.)	2·008 ± 0·005	35	—

* Δ_{HH} = full width at half-height. † Δ_{MS} = width between points of maximum slope.

evolution of oxygen occurred but there was no detectable coloration. The concentration of radicals was probably in excess of 10^{-4}M under good conditions: it did not appear to depend crucially upon the degree of purification.

Irradiation.—Specimens for spectrophotometric and electron spin resonance analysis were prepared and irradiated as described earlier.[14,16] A medium pressure 250 w mercury arc lamp was used, the light being filtered through several thicknesses of soda-glass so that only the

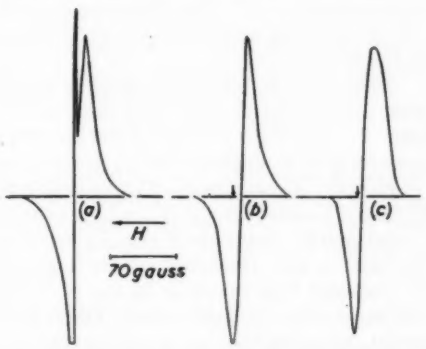


FIG. 3. *Electron resonance spectra: (a) sodium ozonide with diphenylpicrylhydrazyl, (b) sodium ozonide alone, (c) glass composed of sodium and potassium hydroxides, water, and hydrogen peroxide after irradiation. The curves are first derivatives of the signal and the arrow indicates the value* $g = 2{\cdot}003$.

3650 Å band and possibly some of the 3130 Å band were effective. Good glasses were obtained from equimolar mixtures of potassium and sodium hydroxide solutions (*ca.* 8M) to which a few drops of hydrogen peroxide had been added immediately before cooling in liquid oxygen.

On irradiation a yellow colour rapidly developed, and an intense electron spin resonance signal was obtained after a few minutes' exposure. The rate of photolysis, however, rapidly decreased, possibly because of the internal filter effect of the coloured species. The ultraviolet spectrum of a glass irradiated for 6 hr. showed considerable absorption in the 370 mμ region (Fig. 2) as well as a peak at 435 mμ, and the electron spin resonance spectrum was broader and less symmetrical than that obtained initially.

On warming to −50° the colour and signal decayed relatively slowly in marked contrast with the behaviour of reactive radicals described previously.[14] This evidence of stability means that radicals such as OH of O^- should not be considered as possible causes of the colour or paramagnetism.

DISCUSSION

Structure of the Ozonide Ion.—Our spectrophotometric and electron spin resonance results confirm earlier evidence that the alkali-metal ozonides are salts containing the ion O_3^-. This ion has the same number of valency electrons as chlorine dioxide, and the electronic structure is probably similar to that suggested for chlorine dioxide by Walsh,[18] though the

[18] Walsh, *J.*, 1953, 2266.

more detailed description given by Bennett, Ingram, and Schonland [13] is not appropriate since low-lying *d*-orbitals are not available for bonding in O_3^-. The first electronic transitions are remarkably similar, since chlorine dioxide has a series of bands in the 370 mμ region with a maximum extinction coefficient of about 2000.[19] This transition is described by Walsh [18] as

$$(a_2'')^2\,(b_2')^2\,(b_1')^2\,(b_1'') \longrightarrow (a_2'')\,(b_2')^2\,b_1')^2\,(b_1'')^2$$

and this formulation is presumably applicable to the spectrum of O_3^-. Using arguments similar to those given,[19] one would expect a smaller energy for this transition in O_3^- since the electron affinity of oxygen is greater than that of chlorine.

Despite the relatively high energy of this transition the fact that the *g*-value is appreciably different from the free spin value means that spin–orbit coupling is not negligible. The apparent absence of *g*-value variation must mean that $g_x \doteqdot g_y \doteqdot g_z = 2{\cdot}012$. This result can be compared with that for chlorine dioxide, for which the values $g_x \doteqdot g_z = 2{\cdot}02$ and $g_z = 2{\cdot}01$ are reported.[13]

The electron spin resonance spectrum for ozonide is very different from that for superoxide, which has a pronounced shoulder on the low-field side. A large variation in *g* is often observed for molecules having axial symmetry: the peak is due to molecules whose axes are nearly perpendicular to the applied field ($g_\perp$) whilst the shoulder is due to molecules nearly parallel ($g_\parallel$). The difference in intensity arises because there is a far greater probability of finding molecules with axial symmetry nearly perpendicular than nearly parallel to the fields.

Absence of detectable asymmetry from the electron spin resonance spectrum obtained from ozonide means that there is no axial symmetry. This means that the ion must be bent, as expected for molecules with 19 valency electrons,[18] and also that the unpaired electron is in an orbital which is spread over the whole ion.

Reaction Mechanisms.—The radical intermediate formed during the decomposition of hydrogen peroxide in alkali can be reasonably identified as ozonide rather than superoxide. Unfortunately, insufficient radicals were accumulated for spectrophotometric study, but the electron spin resonance results seem conclusive. The mechanism involved is obscure. We consider that catalysis by traces of impurities is important. Many transition-metal ions are oxidised to high valency states by hydrogen peroxide in alkaline solution, and the resulting oxyions then act as catalysts for the decomposition of hydrogen peroxide to oxygen and water, being themselves reversibly reduced during the process.[20] This reaction is thought to proceed by single electron-transfer stages and hence to involve free radicals. Since oxygen is a product, and in view of the stability of the ozonide ion, we suggest that steps such as (1), (2), and (3) are important, and that relatively large stationary concentrations of ozonide may accumulate:

$$O_2 + OH \rightleftharpoons HO_3 \quad \ldots\ldots\ldots\

Forchheimer and Taube,[21] using more dilute alkali, found that exchange of ^{18}O between water and oxygen was catalysed by ozone. One interpretation put forward was that the exchange

$$^{*}OH^{-} + OH \longrightarrow {}^{*}OH + OH^{-} \quad . . . . . (4)$$

was followed by steps (1), (2), and (3). The hydroxyl radicals in (4) are derived from ozone.[21] In view of the remarkable stability of solid ozonides we prefer this sequence for the exchange to the one involving the reverse of reaction (3), which was postulated originally.[21]

These reactions are probably significant also in the reaction between ozone and solid hydroxides, which could be initiated by the charge-transfer (5), followed either by (1) and (2), or (6) and (3).

$$O_3 + OH^{-} \rightleftharpoons O_3^{-} + OH \quad . . . . . (5)$$

$$OH + OH^{-} \rightleftharpoons O^{-} + H_2O \quad . . . . . (6)$$

Step (5) is energetically unfavourable, but nevertheless hydroxide in the absence of an excess of water is a relatively powerful reducing agent, since it reacts with manganate to give hypomanganate [20] and chromate to give hypochromate.[23]

Again the same separate stages are probably involved in the reaction between solid potassium ozonide and water.[24] The apparent independence of pH is possibly a result of the experimental method,[24] since most of the rapid reaction will have occurred close to the dissolving solid, and therefore in an environment largely independent of the bulk solvent.

Photolyses.—Since hydrogen peroxide and the hydroperoxide ion have very similar ultraviolet spectra and on photolysis decompose remarkably similarly,[25] the primary act of light absorption probably leads directly to (7) rather than being a photoionisation:

$$HO_2^{-} + h\nu \longrightarrow O^{-} + OH \quad . . . . . (7)$$

If this is so, then the very rapid build up in the concentration of ozonide must mean that this is an efficient step even in a rigid glass, and also that radical migration can occur so that steps (6) and (3) can be realised. Once the available oxygen in the glass has been consumed, however, it is probable that a build-up in the concentration of superoxide would occur, as a consequence of reactions such as (8).

$$O^{-} + HO_2^{-} \longrightarrow OH^{-} + O_2^{-} \quad . . . . . (8)$$

The results [Figs. 2 and 3(*c*)] reveal that there is some evidence, from the ultraviolet and electron spin resonance spectra of glasses irradiated for extended periods, for this contention.

Thanks are due to Dr. J. Bennett, Dr. J. F. Gibson, and Dr. D. J. E. Ingram for some early electron spin resonance measurements, and to Dr. C. A. McDowell for hospitality to one of us (M. C. R. S.) during the tenure of a Visiting Associate Professorship at the University of British Columbia. Grants from D.S.I.R. (to A. D. McL.) and Courtaulds Ltd. (to M. G. T.) are acknowledged.

UNIVERSITY OF BRITISH COLUMBIA, VANCOUVER, CANADA.
THE UNIVERSITY, SOUTHAMPTON (*present address*, M. C. R. S.). [*Received, October 20th*, 1958.]

[23] Bailey and Symons, *J.*, 1957, 203.
[24] Kasarnowsky, Lipichin, and Tichomirov, *Nature*, 1956, **178**, 100.
[25] Baxendale and Wilson, *Trans. Faraday Soc.*, 1957, **53**, 344.

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194. *Unstable Intermediates. Part VI.* Spectra of Certain Aryl Carbinols and Olefins in Strongly Acidic and Weakly Acidic Media.*

By J. A. Grace and M. C. R. Symons.

An attempt has been made to find conditions under which reactive carbonium ions have sufficient life for spectrophotometric study. It is concluded that stable dilute solutions in sulphuric acid can be prepared provided precautions are taken to avoid interaction between carbonium ions and parent molecules during preparation. The compounds studied include benzyl alcohol and styrene, α-methylstyrene, and the corresponding carbinols. Under certain conditions these compounds give rise to intense absorption in the visible region of the spectrum in weakly acidic media. These spectra, which are quite different from those attributed to carbonium ions, are recorded and the nature of the solutions discussed.

Carbonium ions are frequently postulated as being transient intermediates in chemical reactions, their presence being inferred from studies on the course of the reactions.[1] Stable carbonium ions, such as the triarylcarbonium ions and certain protonated fused ring aromatic compounds,[2] have been studied extensively in a variety of solvents. Diarylcarbonium ions are also known, though they are reported to be unstable, but very few monoarylcarbonium ions have been studied as such.

Our main purpose has been to prepare monoarylcarbonium ions in conditions such that they can be studied by spectrophotometric and other methods, the basic assumption being that the reason for their usual transient life-time is not that they are unstable, but that they are highly reactive electrophils.

Several of the compounds selected form coloured solutions in solvents such as acetic–sulphuric acid mixtures. The spectra of these solutions are recorded and some properties listed.

Experimental and Results

Materials.—Sulphuric acid and oleums were purified as described earlier.[3] "AnalaR" benzene was shaken repeatedly with sulphuric acid, then washed with purified water, dried with sodium, and distilled. *cyclo*Hexane and chloroform (B.D.H. Spectrograde) were purified similarly.

αα-Dimethylbenzyl alcohol, prepared from acetone and phenylmagnesium bromide, had b. p. 52°/3 mm. α-Ethyl-α-methylbenzyl alcohol, prepared similarly, had b. p. 75°/2 mm. Anthracene (B.D.H. microanalytical reagent) was not further purified. 9-Methylanthracene, prepared from anthracene-9-aldehyde, had m. p. 79·5°.[4] Other solvents and solutes were high-grade commercial products further purified by standard methods.

Preparation of Solutions in Sulphuric Acid.—An attempt to prepare stable solutions of reactive carbonium ions can succeed only if the concentrations of all compounds with which they can react is a minimum. The reactants selected were olefins and the corresponding alcohols; both are attacked by electrophils and a preparative procedure was sought in which contact between carbonium ions and reactants was avoided. This was finally achieved by procedures (1*a* and *b*) (below), and hence reactions such as disproportionation and polymerisation were avoided. Sulphonation was likewise avoided since the rate of sulphonation of carbonium ions, in contrast to that of the corresponding alcohols or olefins, is slow.

The only other reaction likely to give coloured species is oxidation, by sulphuric acid, to the corresponding radical-ions[5] or carbonyl compounds. Electron spin resonance studies

* Part V, preceding paper.

[1] (*a*) Bethell and Gold, *Quart. Rev.*, 1958, **12**, 173; (*b*) Gillespie and Leisten, *ibid.*, 1954, **8**, 40.
[2] Reid, *J. Amer. Chem. Soc.*, 1954, **76**, 3264.
[3] Symons, *J.*, 1957, 387.
[4] Phillips and Cason, *J. Amer. Chem. Soc.*, 1952, **74**, 2934.

showed that the solutions were not paramagnetic, thus eliminating the former, and an examination of the spectra of relevant carbonyl compounds eliminated the latter. (Bands having $\varepsilon_{max.} \simeq 10^4$ were detected, with maxima at 345, 347, 352, and 411 mμ for benzophenone, acetophenone, anthrone, and anthraquinone respectively, in sulphuric acid.)

Procedure (1*a*). Dilute solutions of the reactant in acetic acid were treated with a hundredfold excess of cold sulphuric acid so that rapid mixing was ensured.

Procedure (1*b*). Solutions of reactant in *cyclo*hexane (10^{-4}M) were cooled in ice and extracted with cold sulphuric acid.

Solutions of benzyl alcohol in sulphuric acid (10^{-5}M) obtained by procedure (1*a*) had spectra which showed little change after 30 min. However, procedure (1*b*) gave solutions which were cloudy and had a rising absorption in the 400 mμ region, not found for the former solutions. The ultraviolet absorption increased slowly and the original orange colour changed to brown

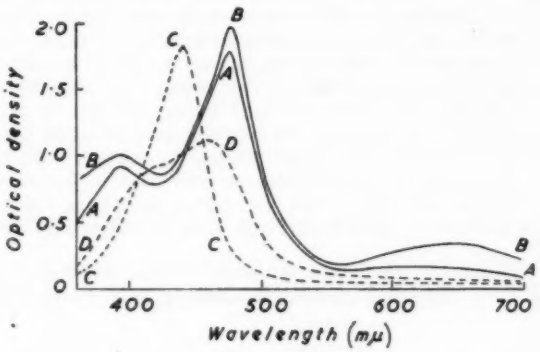


FIG. 1. *Absorption spectra for acid solutions of diphenylmethanol.*

A, By use of procedure (2*a*) after 5 min.
B, By use of procedure (2*a*) after 3 hr.
C, By addition of acetic acid to a solution in sulphuric acid after 5 min.
D, By addition of acetic acid to a solution in sulphuric acid after 6 hr.

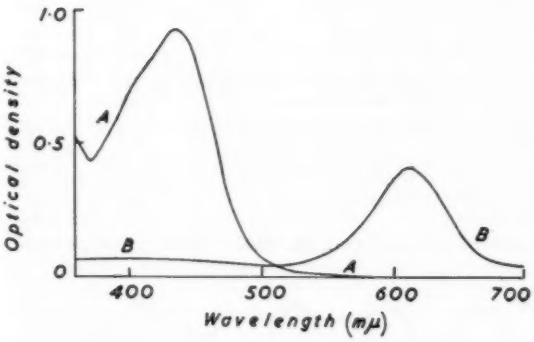


FIG. 2. *Absorption spectra of styrene in sulphuric acid* (100%) (*A*), *and in sulphuric–acetic acid mixtures* [*procedure* (2*b*)] (*B*).

on standing. It seems probable that, despite the precautions taken, polymerisation was occurring.[5]

The usual procedures for obtaining solutions in sulphuric acid, such as direct solution of the parent compound or extraction from more concentrated solutions, proved unsatisfactory.

Extinction coefficients could not always be measured accurately, but in all cases they were established to within 10% of the true value. The high values obtained (*ca.* 10^4) are of the same order as those found for carbonium ions by other workers. Such values preclude the possibility that traces of impurities are responsible for the spectra recorded.

Preparation of Solutions in Weakly Acidic Media.—Solutions in benzene containing trichloroacetic acid (*ca.* 2 mole $l.^{-1}$) were prepared by direct dissolution of the carbinol or hydrocarbon, the resulting solutions being exposed to light for a minimum period. Solutions in acetic–sulphuric acid mixtures were prepared as follows:

Procedure (2*a*). A mixture of sulphuric and acetic acids (1 : 1 v/v) was added dropwise,

[5] Shiner and Berger, *J. Org. Chem.*, 1941, **6**, 305.

with stirring, to a cooled dilute solution of the compound in acetic acid. Spectra were recorded at intervals during the addition.

Procedure (2*b*). Ice-cold solutions of the compound in sulphuric acid, prepared by procedure (1*a*) or (1*b*) but somewhat more concentrated than usual, were poured into cold acetic acid or acetic–sulphuric acid, the solutions being cooled in a bath at $-80°$ during the addition. When solutions were prepared by procedure (2*b*) comparison with the corresponding spectra of solutions in sulphuric acid was possible (see Fig. 2). From such comparisons we conclude that the extinction coefficients for the bands in the 500—600 mμ region recorded in Table 2 are $\fallingdotseq 10^4$, and generally greater than the extinction coefficients for bands recorded in Table 1 and attributed to carbonium ions.

Results are recorded in Table 2. Details for certain compounds are as follows: When anthracene was subjected to procedure (2*b*) only colourless solutions resulted. Procedure (2*a*) gave very pale blue colours unless nearly saturated solutions were used, when, at times, remarkably intense blue colours resulted, the intensity increasing with time. It seemed possible that this colour was due to anthracene positive ions,[8,15] but no electron spin resonance absorption was detected at either room or liquid-oxygen temperatures. [Checks were made on other coloured solutions obtained by procedures (2*a*) and (2*b*), with similar results.]

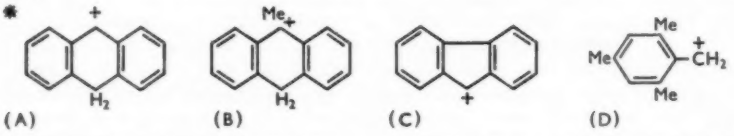
Styrene and α-methylbenzyl alcohol, treated by procedure (2*a*), gave cloudy, colourless solutions. In contrast, the blue solutions obtained by procedure (2*b*) were quite clear, and stable in the absence of light, though the colour was discharged on adding water.

Solutions of α-methylstyrene and αα-dimethylbenzyl alcohol became red when either procedure was used. However, a band at 390 mμ, attributed to the ion $PhC^+(Me)_2$, was found in addition to the 480 mμ band when procedure (2*a*) was used.

TABLE 1. *Absorption maxima for long-wavelength bands of solutions of various carbinols and hydrocarbons in sulphuric acid, prepared by procedures* (1*a*) *and* (1*b*).

Compound	Possible carbonium ion *	$\lambda_{max.}$ (mμ) †	$\varepsilon_{max.}$	Compound	Possible carbonium ion *	$\lambda_{max.}$ (mμ) †	$\varepsilon_{max.}$
Anthracene	A	427	3×10^4	$Ph{\cdot}CMe_2{\cdot}OH$	$Ph{\cdot}\overset{+}{C}Me_2$	390	$\fallingdotseq 10^4$
		425 [a]	$3{\cdot}1 \times 10^4$	$Ph{\cdot}CMe{\cdot}CH_2$	,,	390	$\fallingdotseq 10^4$
9-Methylanthracene	B	412	3×10^4	$Ph{\cdot}CHMe{\cdot}OH$	$Ph{\cdot}\overset{+}{C}HMe$	435	$\fallingdotseq 10^4$
				$Ph{\cdot}CH{=}CH_2$	—	435	$\fallingdotseq 10^4$
$Ph_2CH{\cdot}OH$	$Ph_2\overset{+}{C}H$	442	4×10^4	$Ph{\cdot}CMeEt{\cdot}OH$	$Ph{\cdot}\overset{+}{C}MeEt$	405	$\fallingdotseq 10^4$
		442 [b]	$5{\cdot}3 \times 10^4$	$Ph{\cdot}CH_2OH$	$Ph{\cdot}\overset{+}{C}H_2$	$\fallingdotseq 470$	$>3 \times 10^3$
$Ph_2C{=}CH_2$	$Ph_2\overset{+}{C}Me$	429 [a]	$3{\cdot}1 \times 10^4$	9-Hydroxyfluorene	C	660 and 480	$3{\cdot}1 \times 10^3$ and 2×10^3
		425 [c]	$3{\cdot}1 \times 10^4$				
$Ph_2CMe{\cdot}OH$	,,	429 [a]	$3{\cdot}1 \times 10^4$				

[a] Ref. 10. [b] Branch and Walba, *J. Amer. Chem. Soc.*, 1954, **76**, 1564. [c] Evans, *J. Appl. Chem.*, 1951, **1**, 240.



† Carbonium ions in solvent HF have similar spectra, but there is a solvent shift of about 15 mμ to shorter wavelengths compared with spectra in H_2SO_4 (cf. ref. 2).

Diphenylmethanol in benzene–trichloroacetic acid gave spectra which closely resembled 1 : 1-diphenylethylene in the same solvent.[6] Fresh solutions were colourless, but a peak at 660 mμ slowly developed which, together with a rising absorption in the 400 mμ region, imparted an emerald-green colour to the solution. As with 1 : 1-diphenylethylene, the band in the 430 mμ region ascribed to the carbonium ion was not observed.

Fig. 1 gives a typical spectrum for solutions of diphenylmethanol obtained by procedure (2*a*). The band at 650 mμ corresponds to the band at 660 mμ for solutions in benzene–trichloroacetic acid, but the bands at 480 and 395 mμ are not characteristic of the carbonium ion (see

[6] Evans, Jones, and Thomas, *J.*, 1957, 104.

Table 1). Treatment of a solution in sulphuric acid with a small quantity of acetic acid gave a solution whose spectrum slowly changed from that of the carbonium ion to that displayed in Fig. 1, which has bands at 480, 440, and 395 mμ, but no band at 650 mμ. Addition of more acetic acid further increased the 480 and 395 mμ bands at the expense of the 440 mμ band.

In order to learn more about these involved changes in spectra the following experiments were devised: (*a*) Green solutions of diphenylmethanol in benzene–trichloroacetic acid, which had been kept until there was no further change in the spectrum, were shaken with a excess of purified water and the colourless benzene layer separated, dried (Na_2SO_4), and filtered. On addition of a solution of trichloroacetic acid in benzene an intense green colour developed

TABLE 2. *Absorption maxima for long-wavelength bands of solutions of various carbinols and hydrocarbons in weakly acidic media.*

	$\lambda_{max.}$ (mμ) in solvent			$\lambda_{max.}$ (mμ) in solvent	
Compound	$CCl_3{\cdot}CO_2H + C_6H_6$	$AcOH + H_2SO_4$	Compound	$CCl_3{\cdot}CO_2H + C_6H_6$	$AcOH + H_2SO_4$
Anthracene ...	750, 590	615 (2*a*)	$Ph{\cdot}CMe{=}CH_2$	No visible bands	480 (2*a*)
$Ph_2CH{\cdot}OH$ ...	660	650, 480, 395 (Fig. 1)	$Ph{\cdot}CHMe{\cdot}OH$	,, ,,	610 (2*a*, 2*b*)
$Ph_2C{=}CH_2$ ...	607 -	600 *	$Ph{\cdot}CH{=}CH_2$ ...	,, ,,	615 (2*a*)
$Ph{\cdot}CMe_2{\cdot}OH$	No visible bands	480 (2*a*, 2*b*)	$Ph{\cdot}CH_2{\cdot}OH$ ...	,, ,,	†

* Ref. 6. † Cloudy solution.

TABLE 3. *Effect of methyl substitution on trigonal carbon.*

Δ (mμ) = ($\lambda_{max.}$ for $R_2\overset{+}{C}H$) − ($\lambda_{max.}$ for $R_2\overset{+}{C}Me$).

$R_2\overset{+}{C}H$	$Ph_2\overset{+}{C}H$	A *	$Ph{\cdot}\overset{+}{C}HMe$	$Ph{\cdot}\overset{+}{C}H_2$	D* †	$(p\text{-}Me{\cdot}C_6H_4)_2\overset{+}{C}H$	$(p\text{-}MeO{\cdot}C_6H_4)_2\overset{+}{C}H$	$(p\text{-}Cl{\cdot}C_6H_4)_2\overset{+}{C}H$
Δ	15	15	45	≒ 35	100	15	17	19

* See footnote to Table 1. † Ref. 12 gives data for $R\overset{+}{C}H_2$ and $R\overset{+}{C}Me_2$ (R = mesityl). Hence the Δ value of 100 should be halved to give a rough measure of the effect for a single methyl group.

immediately, and a spectrophotometric examination showed that the spectra of the original solutions were quantitatively reproduced.

(*b*) A solution of diphenylmethanol in sulphuric–acetic acid, whose spectrum was dominated by the 480 and 395 mμ bands, was poured on ice, and the colourless solution extracted with benzene. After separation and drying, the benzene extract was added to trichloroacetic acid–benzene, and the spectrum of the resulting pink solution recorded. The peaks at 480 and 395 mμ were still present, and there was no absorption in the 660 mμ region. The identity of the species absorbing at 480 mμ is unknown, and will not be considered at this stage. This experiment establishes that the species absorbing at 660 mμ is not derived from the former compound.

(*c*) Bisdiphenylmethyl ether was prepared from diphenylmethanol as crystals from acetic–perchloric acid.[7] On dissolution in benzene–trichloroacetic acid the ether behaved in just the same way as the carbinol.

Stable solutions of benzyl alcohol could not be obtained by any of the procedures outlined above.

Spectra.—The spectra were recorded on a Unicam S.P. 600 glass or S.P. 500 quartz spectrophotometer, pure solvents being used as reference solutions. Generally, solutions were kept in stoppered 1 cm. quartz cells. The results are summarised in Tables 1—3, and representative examples are displayed in the Figures. Generally, only the low-energy band maxima are recorded in the Tables. In many cases other bands were detected in the near-ultraviolet region, but they were not studied systematically.

DISCUSSION

Although several of the carbonium ions are thought to be important intermediates in a variety of reactions, no direct study has previously been reported. The postulate that the spectra (Table 1) are due to carbonium ions can be supported as follows: (*a*)

[7] Burton and Praill, *J.*, 1953, 986.
[8] Carrington, Dravnieks, and Symons, *J.*, 947.

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Identical spectra were obtained from alcohols and corresponding olefins, (*b*) extinction coefficients and wavelengths are very similar to those of stable carbonium ions, (*c*) characteristic changes in spectra on methyl substitution (Table 3) parallel the trends for more stable carbonium ions. Other evidence is given in the Experimental section. The reproducibility of the spectra shows that complete conversion is achieved under our conditions.

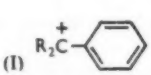
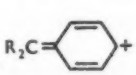
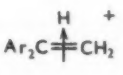
Effect of Methyl Substitution.—We consider only ions which have the chromophore $>\overset{+}{C}-Ph$, and the substitution is of the type $R-\overset{+}{C}H-Ph \longrightarrow R-\overset{+}{C}Me-Ph$.

For diarylcarbonium ions, whose structure can be assumed, the trends are all very similar, involving a shift of about 15 mμ to shorter wavelengths. For anthracene and 9-methylanthracene the fact that a similar shift is observed can be understood in terms of Gold and Tye's concept, who pointed out that anthracene protonated at position 10 closely resembles the diphenylmethyl carbonium ion.[10,11]

By analogy, we expected a similar shift for monoaryl carbonium ions. In fact, the shift is in the same direction but considerably larger (Table 3).

These trends make a consistent picture. Without considering the nature of the long-wavelength transition in detail it seems reasonable to suggest that there is a partial transfer of charge from the ring to the tervalent carbon atom, so that the structure (I) contributes considerably to the ground state, whilst structures such as (II) are of greater importance in the excited state. In that case when R is methyl, both ground and excited states will be more stable than when R is hydrogen, but the stabilisation will be greater for the ground than for the excited state and hence the transition energy will be greater.

In accord with this pictorial representation is the fact that replacement of hydrogen by methyl in the *para*-position of the aromatic ring results in a shift of the band to *lower* energies.[6,12] Replacement of hydrogen by methyl in the *ortho*-positions leads to steric interactions which add greatly to the complexity of the problem.[13]

(I)  (II)   (III)

Spectra in Weakly Acidic Media.—This section has only reached a preliminary stage and is still being studied. However, in view of current interest in π-complex formation, and the postulate by Evans and his co-workers [6] that the bands in the 600 mμ region of certain diarylethylenes in weakly acidic solvents are due to complexes in which protons are π-bonded to the olefinic bonds, we consider that the present results should be reported. The structure proposed [6] (III) was arrived at by a process of elimination. One cannot be certain that all possibilities were considered, and the properties reported [6] are not in accord with current theories about such complexes. The remarkable similarity between the behaviour of 1 : 1-diphenylethylene [6] and diphenylmethanol suggests that there may be some alternative explanation, since there is no way of deriving a complex of the type shown above from the latter compound.

The phenomenon seems to be broad, requiring a comprehensive interpretation; many have been examined but none has proved comprehensive.

THE UNIVERSITY, SOUTHAMPTON. [*Received, September 5th*, 1958.]

[9] Weissman, Conradi, and de Boer, *J. Chem. Phys.*, 1957, **26**, 963.
[10] Gold and Tye, *J.*, 1952, 2172.
[11] Lewis and Symons, *Quart. Rev.*, 1958, **12**, 230.
[12] Deno, Jaruzelski, and Schriesheim, *J. Org. Chem.*, 1954, **19**, 155.
[13] Newman and Deno, *J. Amer. Chem. Soc.*, 1951, **73**, 3648.

195. *Unstable Intermediates. Part VII.* Nuclear Magnetic Resonance Studies of Solutions of Iodine in Oleum.*

By T. M. Connor and M. C. R. Symons.

The proton nuclear resonance absorption band for solutions of iodine in oleum is much broader than that for oleum alone, and is shifted to higher fields. The shift and broadening are approximately proportional to the molar concentration of iodine from 0·1 to 0·4M. These changes are interpreted in terms of the formation of a paramagnetic species for which a magnetic moment of about 1·5 B.M. is estimated on the arbitrary assumption that all the iodine is converted into this species. The results are discussed in terms of the postulate that the paramagnetic species is the iodine cation.

Iodine reacts with concentrated oleum to give blue solutions in which iodine is largely in the +1 valency state and which are powerful iodinating agents.[1] It was tentatively suggested that iodine cations are present in these solutions and, since the ground state for these ions is considered to be $^3P_2$, that these ions are responsible for the paramagnetism. Since there was no way of estimating the concentration of these ions, a magnetic moment was calculated on the arbitrary basis of complete conversion. A mean value of 1·9 B.M. was estimated for 0·1M-solutions.

Spectrophotometry showed that these solutions had four bands in the 200—1000 mμ region. Since the $^3P_2 \rightarrow {}^1D_2$ transition for iodine cations should be found in the 700 mμ region,[2] the 640 mμ band was assigned to the iodine cation and the remaining bands to other species containing iodine.[2] These results showed that a considerable quantity of the iodine was present in one or more forms other than as the bare cation, and hence that the real magnetic moment for this ion should be considerably greater than 1·9 B.M. Unfortunately, there seems to be no way of predicting accurately the magnitude of the magnetic moment for I^+ in solution: the " spin-only " value would be 2·83 B.M. but there is no compelling reason for assuming this value.

Nuclear resonance studies were undertaken to provide independent proof of the presence of a paramagnetic species, in view of the very small changes in weight upon which earlier calculations were based,[1] and because a consideration of the results in detail might provide further evidence about the presence of iodine cations.

All attempts to observe electron spin resonance spectra for these solutions have failed, although solid solutions covering a wide concentration range have been studied at 20° K. If the paramagnetic species is indeed the iodine cation, this result is reasonable, since one would expect considerable zero-field splitting of the energy levels in addition to marked spin–orbit coupling for a ^3P ground state. Hence a single magnetically diluted crystal would be a minimum requirement for a successful study and all attempts to prepare such crystals have failed.

Nuclear resonance is not usually considered as a technique suitable for the detection of paramagnetic species in small concentration. However, in cases of this sort, when electron spin resonance fails, nuclear resonance may often be used, although the sensitivity is far smaller. When proton resonance absorption bands are studied in solutions containing various concentrations of paramagnetic ions there is generally a marked shift in addition to an increased intensity and broadening.[3,4] These phenomena are characteristic, and the data can be used to estimate a value for the magnetic moment which is generally very close to the static magnetic moment of the ion.

* Part VI, preceding paper.

[1] Symons, *J.*, 1957, 387.
[2] Symons, *J.*, 1957, 2186.
[3] Wertz, *Chem. Rev.*, 1955, **55**, 829.
[4] Dickinson, *Phys. Rev.*, 1951, **81**, 717.

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Experimental

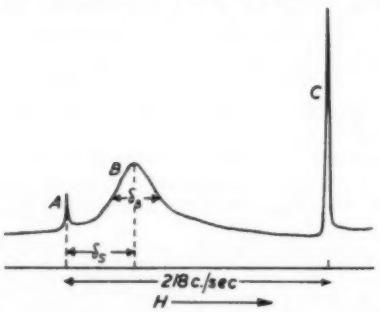
The proton nuclear resonance spectra of solutions of iodine in 65% oleum were measured at 40 Mc./sec. by using a Varian 4300 high-resolution spectrometer. The samples were contained in tubes of 5 mm. outside diameter which were spun to reduce effective field inhomogeneities. Two external reference capillaries were included with each sample, one containing pure 65% oleum and the other distilled water, enabling the shifts and broadening of the oleum resonances to be found by interpolation. Owing to the width of some of the oleum signals this was a more convenient method of measuring shifts than the usual side-band technique which was however used to measure the distance between the two reference capillaries. This was found to be 218 c./sec., the oleum lying on the low-field side.

The oleum was not specially purified.[3] The line-width of the signal obtained was about 2 c./sec., indicating the absence of any appreciable quantity of paramagnetic impurities. The iodine was " AnalaR."

Table 1. *Broadening and chemical shift due to the presence of* I_2.

Concn. (mole/l.)	Line-width at ½ height (c./sec.)	Broadening (c./sec.)	Shift from 65% oleum (c./sec.)	Concn. (mole/l.)	Line-width at ½ height (c./sec.)	Broadening (c./sec.)	Shift from 65% oleum (c./sec.)
Pure oleum	2	0	0	0·2003	24	22	29
0·00985	4	2	0	0·3136	34	32	43
0·0197	4	2	0	0·401	41	39	56
0·0281	7	5	2	Saturated	75	73	104
0·0985	14	12	14·5				

A typical spectrum for a 0·401M-solution of iodine in 65% oleum is shown in the Figure. The widths of the oleum resonances at half-height and their shifts to higher field with respect to the pure oleum reference signal are tabulated as a function of iodine concentration (Table 1).



Proton nuclear resonance spectrum of iodine (0·401M) *in oleum* (65%).
A, 65% Oleum reference.
B, Iodine solution.
C, Water reference.

The proton resonance spectra of brown solutions obtained by dissolving iodine in 20% oleum were also examined and showed no appreciable broadening or shift. It is therefore concluded that these solutions do not contain paramagnetic species, a result in accord with previous findings.[1,2] The broadening was determined by subtracting the line-width due to pure oleum (2 c./sec.) from the line-width at half-height found for the solutions. The shift and broadening are approximately proportional to the iodine concentration (Table 1) although the broadening falls off at high iodine concentrations.

Discussion

Shift.—Dickinson [4] showed that the variation of chemical shift with concentration is given by

$$d\delta_s/dc = -2\pi\chi H_0/3 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where δ_s is the chemical shift, c the concentration, and χ the susceptibility of a particular solution. H_0 is the field in the magnet gap, 9·4 kilogauss. This expression requires that: (*a*) the sample shape approximates to an " infinite cylinder "; (*b*) the field due to the remaining ions in the Lorentz cavity is zero. The approximation (*a*) is good in this case (dimensions 60 mm. × 3·5 mm.). Dickinson [4] found deviations from eqn. (1) which he

interpreted in terms of a non-zero Lorentz cavity field. In this case the field will be assumed to be zero. Since

$$\chi = N\beta^2\mu^2/3kT \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where β is the Bohr magneton and μ is the effective magnetic moment of I^+, the slope, $d\delta_s/dc$, can be expressed in terms of μ.

The data of Table 1 give −72 cycles/mole/l. for $d\delta_s/dc$. This gives $\mu = 1{\cdot}5$ B.M. on the arbitrary assumption that all the iodine is present as I^+, *i.e.*, that the reaction $I_2 \longrightarrow 2I^+ + 2e$ goes to completion. This result may be compared with the value of 1·9 B.M. found previously for 0·1M-solutions by using a conventional Gouy balance.

Although this result qualitatively confirms the earlier measurements independently, there is not quantitative agreement. Deviations from equation (1) are often found and have been explained in two ways. Bloembergen and Dickinson [5] developed an expression which takes into account possible magnetic anisotropy. Since spin–orbit coupling is expected for the iodine cation, this could cause the discrepancy. On the other hand, marked deviations from eqn. (1) can occur if covalent bonding between the paramagnetic species and the compound containing the resonating nucleus gives rise to a finite density of unpaired electrons at the nucleus.[6,7] The latter effect may be so important that the direction of shift is reversed. The deviation described here is relatively small and this mechanism can hardly play an important rôle. This conclusion is in agreement with the postulate that iodine cations are present, and eliminates certain protonated paramagnetic species such as HI^+ or HI_2^{2+}.

Broadening.—For a Lorentzian line shape, the line-width at half-height in cycles/sec., δ_B, is related to the spin–spin relaxation time, T_2, by the expression

$$\delta_B = 1/\pi T_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

For solutions, T_2 and T_1, the spin–lattice relaxation-time, can normally be assumed to be equal. To test this assumption, T_1 for a 0·4M-solution of iodine in oleum (65%) was measured directly, using spin-echo techniques,[8] to be $7 \pm 1{\cdot}5$ μsec., which is very close to the value of 8·15 μsec. calculated from the line-width at this concentration, thus showing that the above assumption is valid in this case.

Bloembergen, Purcell, and Pound's [9] original expression relating T_1 to the magnetic moment of the paramagnetic ions was modified by Abragam [10] to

$$1/T_1 = 16\pi^2 N_{ion}\mu^2\gamma^2\eta\beta^2/15kT \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

where N_{ion} is the concentration of paramagnetic ions in moles/c.c., γ is the magnetogyric ratio for the proton, and η is the viscosity.

TABLE 2. *Viscosity of* I_2–65% *oleum solutions.*

Solution	Average flow time (sec.) (of 4 readings)	Viscosity (centipoises)
65% Oleum	238·6	44·5
0·208M-I_2	244·8	45·6
0·402M-I_2	259·6	48·4

The viscosity was measured at 25° (Table 2), a value of 44·5 centipoises being taken for 65% oleum.[11] There is a small increase in viscosity which would slightly accentuate the deviation from linearity of the graph of broadening against concentration of iodine found at high concentrations (Table 1).

[5] Bloembergen and Dickinson, *ibid.*, 1950, **79**, 179.
[6] McConnell and Holm, *J. Chem. Phys.*, 1958, **28**, 749.
[7] Phillips, Looney, and Ikeda, *ibid.*, 1957, **27**, 1435.
[8] Hahn, *Phys. Rev.*, 1950, **80**, 580.
[9] Bloembergen, Purcell, and Pound, *ibid.*, 1948, **73**, 679.
[10] Abragam, personal communication.
[11] Bright, Hutchison, and Smith, *J. Soc. Chem. Ind.*, 1946, **65**, 385.

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Using equation (4) and the previously calculated value of $\mu = 1{\cdot}5$ B.M., we find the inverse relaxation time to be $7{\cdot}35 \times 10^3$ sec.$^{-1}$ for a 0·4M-solution. The experimental value of $1{\cdot}2 \times 10^2$ sec.$^{-1}$ is far smaller, and the broadening is a factor of 60 less than predicted by eqn. (4). We conclude that this equation is not a satisfactory representation in this case.

An alternative approach is simply to compare the results with similar data for other systems. This can be done by interpolation of the data given by Morgan *et al.*,[12] who measured T_1 for protons in aqueous solutions of chromic ions bonded to a variety of ligands. The viscosity of these solutions was varied over a wide range by addition of glycerol. From the data for $Cr(en)_3^{3+}$ we estimate $T_1 = 0{\cdot}53$ μsec. for a solution 0·4M in chromic ions and having a viscosity of 0·48 poise. Using 3·9 B.M. for the magnetic moment of chromic ions in the ethylenediamine complex, one can then estimate the moment of the paramagnetic species in oleum from

$$T_1(\mathrm{I})/T_1(\mathrm{Cr}) = \mu^2(\mathrm{Cr})/\mu^2(\mathrm{I}) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

The result, 1·1 B.M., is comparable with the results previously obtained, and suggests that the paramagnetic species are affecting the protons of the solvent in similar ways in these solutions. The main conclusion drawn by Morgan *et al.*[12] is that direct proton exchange between the complex ion and the solvent is not occurring. When applied to the iodine solution, this means that species such as HI^+ can again be rejected, but that the postulate that iodine cations are present is in accord with the results.

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University of British Columbia, Vancouver, Canada.
The University, Southampton (*present address*, M. C. R. S.) [*Received, November 3rd*, 1958.]

[12] Morgan, Nolle, Hull, and Murphy, *J. Chem. Phys.*, 1956, **24**, 906.

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196. *The Kinetics of Hydrogen Isotope Exchange Reactions. Part IX.* The Exchange between Cobalt(III) Ammines and Water.*

By H. Block and V. Gold.

The rate of the base-catalysed loss of deuterium from deuterated hexamminocobalt(III) and from deuterated oxalatotetramminocobalt(III) ions to water has been studied as a function of buffer composition, mainly in aqueous acetic acid–acetate buffers of constant ionic strength. Both reactions exhibit specific hydroxide-ion catalysis, in that the rates are proportional to hydroxide-ion concentration and the catalytic coefficient for the acetate ion is indistinguishable from zero. It is argued that the only acceptable mechanism for the exchange involves a rate-determining deuteron transfer from the complex ion to a base, and that the observation of specific catalysis is to be ascribed to a large value of the exponent in the Brønsted catalysis law. The reaction of the oxalatotetrammino-complex is about 20 times slower than that of the hexammine.

The acidity of aqueous solutions of hexamminocobalt(III) salts is discussed in relation to the exchange mechanism. It is concluded that the acidity cannot be due to a rapid proton-transfer equilibrium between the ammine and water, as is generally stated, but that it is due to association between hexamminocobalt(III) and hydroxide ions.

Previous Parts have dealt with acid-catalysed exchange reactions between solute and solvent species, and, in particular, the connection between the form of the catalysis and

* Part VIII, *J.*, 1958, 3904.

the proton-transfer reactions involved in the mechanism. This approach has now been extended to two base-catalysed reactions, *viz.*, the exchange between the solvent (water) and deuterated hexamminocobalt(III) and oxalatotetramminocobalt(III) ions. The former ion [and also the trisethylenediaminecobalt(III) ion] exchange deuterium with the solvent water at a conveniently measurable rate over a certain range of pH values,[1] the rate increases with the pH value,[1] and all ammine hydrogen atoms are exchangeable.[1] The more quantitative conclusions drawn from the earlier work [1] are not so firmly established, as the experimental techniques then available made it expedient to use high concentrations of the ammines and ionic strengths as high as 0·4M. Such values are excessive for the detailed analysis of rate constants required for establishing the presence or absence of general base catalysis. This is particularly serious when, as here, triply charged ions are involved in the reaction.

In the work now reported the loss of deuterium from the partially deuterated ammine to an initially light aqueous buffer solution was followed by examination of the infrared spectra of the cobaltammine ions isolated by precipitation during the course of the reaction. The exchanging substrates were present (as chlorides) at an ionic strength not exceeding 0·02M, and groups of experiments were carried out at constant total ionic strengths up to 0·2M. The results can be analysed without ambiguity.

Experimental

Hexamminocobalt(III) chloride was prepared by oxidation of an ammoniacal solution of cobaltous and ammonium chloride with hydrogen peroxide in the presence of activated charcoal as catalyst.[2] Impurity in the form of aquopentamminocobalt(III) chloride was removed by Anderson, Briscoe, and Spoor's method.[1b] The pure hexammine was washed with water, alcohol, and ether and analysed for ammonia, cobalt(III), and chloride by standard volumetric methods [2] [Found: Cl^-, 40·1; NH_3, 37·5; Co^{3+}, 22·2. Calc. for $Co(NH_3)_6Cl_3$: Cl^-, 39·8; NH_3, 38·1; Co^{3+}, 22·1%].

Deuteration was effected by dissolving the salt in H_2O–D_2O mixtures of the required composition and keeping the solutions for one day at 25°. Complete isotopic equilibrium between solute and solvent is established within this time. The solutions thus obtained were used directly without prior separation of the heavy salt.

Chloroaquotetramminocobalt(III) chloride was prepared and purified according to the procedures described in Gmelin-Kraut's Handbuch.[3]

Oxalatotetramminocobalt(III) chloride was made by treatment of the previous salt with oxalic acid by the established procedure [4] (Found: Cl^-, 14·49; NH_3, 26·92. Calc. for $[Co(NH_3)_4C_2O_4]Cl$: Cl^-, 14·41; NH_3, 27·18%).

Deuteration was accomplished in two ways. Standard samples of the partially deuterated salt with known deuterium content were prepared by equilibrating the salt with D_2O–H_2O mixtures of known composition. Because of the low solubility of the complex, the deuterated samples used in the kinetic experiments were prepared by exchange of the more soluble precursor in the preparation [chloroaquotetramminocobalt(III) chloride] with D_2O–H_2O mixtures on a water-bath. The preparation of the oxalatotetrammine was then completed by treatment with oxalic acid as before. Because of the acidic conditions during this stage of the preparation and purification very little, if any, exchange would occur during these last steps.

The chemical stability of hexamminocobalt(III) chloride and of oxalatotetramminocobalt(III) chloride under the conditions of the exchange experiments was confirmed by measuring the ultraviolet absorption spectra in aqueous buffer solutions covering the pH range studied and finding them to remain unchanged over a substantial period.

Conditions for Kinetic Experiments.—Reactions were carried out at 25°, phosphate and acetate buffers of known composition being used in ordinary water, with the addition of the requisite amount of potassium chloride to bring the total ionic strength of the solution (after addition of the complex salt) to a constant value for each group of experiments.

[1] (*a*) Anderson, James, and Briscoe, *Nature*, 1937, **139**, 507; (*b*) Anderson, Briscoe, and Spoor, *J.*, 1943, 361.
[2] Palmer, "Experimental Inorganic Chemistry," Cambridge, 1954, p. 530.
[3] Gmelin-Kraut's "Handbuch der Anorganischen Chemie," 1909, Vol. V (i), p. 378.
[4] *Op. cit.*, p. 452.

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Stoppered flasks containing the buffer solutions were immersed in the thermostat to attain the required temperature. The deuterated complex was then added in a suitable form, and the exchange allowed to proceed. Portions were removed at intervals and treated with precipitating reagent so as to throw down a suitable derivative for isotope assay. One of the samples was used for pH measurement of the reaction solution, a Cambridge pH meter with a glass electrode being used.

In the case of the hexamminocobalt(III) ion, the required amount of deuterated salt was added to the buffer as a solution (2 ml.) in the D_2O–H_2O solvent used for the preparative exchange, the total volume of the reaction mixture being made up to 100 ml. In this procedure the total concentration of deuterium in the system is sufficiently high for the ammine to contain a small but appreciable amount of deuterium at equilibrium, *i.e.*, at the completion of the kinetic exchange experiments. The isotope assay was performed on the hexamminocobalt(III) toluene-*p*-sulphonate, which was obtained by adding samples of the reaction solution to toluene-*p*-sulphonic acid (20%) in 0·5M-hydrochloric acid. Precipitation was accelerated by cooling ($-10°$ to $-30°$) and vigorous stirring. It was verified that the presence of hydrochloric acid ensured the arrest of the exchange.

For the oxalatotetramminocobalt(III) ion, a weighed amount of the deuterated solid salt (chloride) was added to the reaction solution and quickly dissolved. For isotope assay the ion was precipitated as the naphthalene-2-sulphonate by the use of a saturated solution of naphthalene-2-sulphonic acid in 0·5M-hydrochloric acid.

Preparation of Standard Samples for Isotope Assay.—The two salts examined contain 18 and 12 equivalent hydrogen atoms respectively. A partially deuterated salt will therefore be a mixture of a number of species: the individual members of the mixture may differ not only in the number of deuterium atoms they contain (molecular isotopes), but also in their positions (isomers). The analytical method used is based on measurements of infrared absorption intensities. Since each member of the deuterated mixture will, in general, have a different absorption spectrum, different samples of identical deuterium content may have different absorption intensities at a given wavelength. In the exchange studies the mixtures of interest are those which have the equilibrium distribution of deuterium atoms, since the deuterated starting material for kinetic runs was prepared by equilibration and—if it may be assumed that secondary kinetic isotope effects are negligible—the deuterium loss is random. Standard samples for the construction of a calibration curve were accordingly prepared by individual equilibration of the ammines in D_2O–H_2O mixtures of different composition and subsequent precipitation of the appropriate sulphonates, and *not* by mixing light and heavy salts in known proportions, since such mixtures would contain a non-equilibrium distribution of deuterium. The precipitation was carried out by using a large volume (50—100 times the volume of the sample) of the solution of the sulphonic acid in light water. In this way, the water of crystallisation in the precipitate is essentially light and does not vary in composition from sample to sample. Occluded water could be removed from all samples, without accompanying exchange of the ammine hydrogen atoms, by washing the precipitate with dry acetone followed by rapid vacuum drying (see footnote to Table 1).

Let us now assume that the equilibrium constant for exchange is the same at every position in the ammine and that it is independent of the degree of deuteration of the ammine. This is equivalent to regarding a molecule RH_x with x equivalent exchangeable positions to be equivalent (for equilibrium considerations) to a system of x identical molecules rH each containing one exchangeable position. The equilibrium constant K_s for exchange at one position

$$rH + HOD \rightleftharpoons rD + H_2O; \quad K_s = [rD][H_2O]/[rH][HOD] \quad . \quad . \quad . \quad (1)$$

may thus be considered independently of what has happened in the rest of the molecule.

The fractional abundance of deuterium in the ammine

$$F = \sum_{j=1}^{x} jC_j/xC \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

(where C_j stands for the sum of the molar quantities of all species of formula $RH_{x-j}D_j$, and $C = \sum_{0}^{x} C_j$) may then also be written as

$$F = [rD]/([rD] + [rH]) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

since, on our assumptions, the fractional abundance is the same at each position of the ammine. Combination of equations (1) and (3) then gives

$$F = K_s[\mathrm{HOD}]/([\mathrm{H_2O}] + K_s[\mathrm{HOD}]) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

For a solution made by mixing a moles of H_2O and b moles of D_2O, the molar amounts of H_2O and HOD (y) can be calculated in terms of the equilibrium constant for the disproportionation

$$\mathrm{H_2O} + \mathrm{D_2O} \rightleftharpoons 2\mathrm{HOD}; \quad K = [\mathrm{HOD}]^2/[\mathrm{H_2O}][\mathrm{D_2O}] \quad . \quad . \quad . \quad . \quad (5)$$

which may also be written

$$K = \frac{4y^2}{(2a - y + xCF)(2b - y - xCF)} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

With a knowledge of the numerical values of K and K_s it is then possible to solve equations (4) and (6) for F in terms of a and b. K has [5] the value 3·96 in the liquid phase at 25° and the equilibrium constant K_s for the hexamminocobalt(III) ion, calculated from spectroscopic measurements [6] *via* partition functions, has the value 0·48. These values are very close to those obtained from a consideration of symmetry numbers alone (*viz.*, 4 and $\frac{1}{2}$, respectively). It is possible to use the round values to calculate the " statistical fractional abundance " (F') of the sample. This corresponds to an assumed random distribution of isotopes between water and salt. It is given quite simply by

$$F' = 2b/(2a + 2b + xC) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

and is, in the present case, a good approximation to the true fractional abundance F. The value of K_s for oxalatotetramminocobalt(III) ion is not known, since an accurate analysis of its infrared spectrum has not so far been achieved. The structural similarity of this ion to the hexammine and the close parallelism of their infrared spectra make it probable that K_s would again lie in the range 0·45—0·55, and again the value $\frac{1}{2}$ leading to equation (7) was used. The kinetic measurements did not reveal any feature which caused us to suspect the adequacy of these assumptions.

Isotope Assay by Infrared Absorption Measurements.—" Nujol " mulls of approximately constant composition (7 mg. of ammine sulphonate with 0·2 ml. of " Nujol ") were prepared. The infrared absorptions in the relevant spectral regions (around 4 and 9·9 or 9·6 μ) were then recorded, a Grubb-Parsons S4 double-beam spectrophotometer being used under standardised conditions (slit width, scanning speed, and loop gain). The intensities of absorption maxima in the two regions are, respectively, sensitive and insensitive to the deuterium content, and the latter can thus be used as an internal standard to compensate for variations in concentration and thickness from sample to sample.[7] It was found for both salts that the function

$$G = \log\left(\frac{T_D'}{T_D}\right) \Big/ \log\left(\frac{T_S'}{T_S}\right)$$

(where T_D stands for the transmission at a peak sensitive to deuterium substitution (at 4·0 μ) and T_S for that of the deuterium-insensitive standard peak (at 9·9 μ for the hexammine toluene-*p*-sulphonate and at 9·6 μ for the oxalatotetrammine naphthalene-2-sulphonate, and T_D' and T_S' are respectively the transmissions at one of the absorption minima immediately adjacent to these bands) is a smooth single-valued function of F' for standard samples prepared as above. The calibration curves thus constructed were used to convert observed values of G of precipitated samples of the substrates of kinetic runs into F'. These analyses were generally carried out in duplicate for every point.

One of the calibration curves is given in Fig. 1. It passes through the origin and obeys a cubic law. The shape of the curve may be rationalised as follows: the absorptions at 4·0 μ are due to N–D stretching modes. These frequencies are slightly different for NH_2D, NHD_2, and ND_3 groupings, but are instrumentally not resolved. The intensity of absorption at a wavelength in this region will then be the sum of three different absorptions, each of which will

[5] Kirshenbaum, " Physical Properties and Analysis of Heavy Water," McGraw-Hill, New York, 1951.
[6] Block, *Trans. Faraday Soc.*, in the press.
[7] Gold and Long, *J. Amer. Chem. Soc.*, 1953, **75**, 4543.

be proportional to the abundance of the grouping responsible. In the absence of isotope effects the fractional abundance of the grouping $NH_{3-n}D_n$ is given by the cubic expression $3!F^n(1-F)^{3-n}/n!(3-n)!$ and hence the sum of the three terms of this type, each multiplied by a different absorption coefficient, will produce a cubic dependence of the total absorption intensity on F.

FIG. 1. *Calibration curve for deuterium assay of hexamminocobalt*(III) *toluene*-p-*sulphonate.*

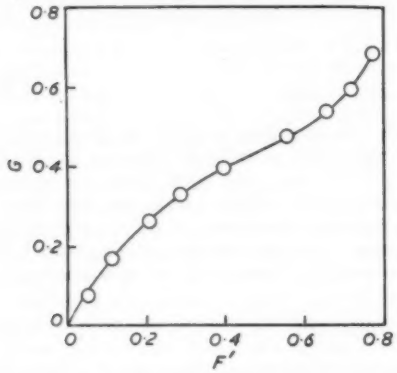
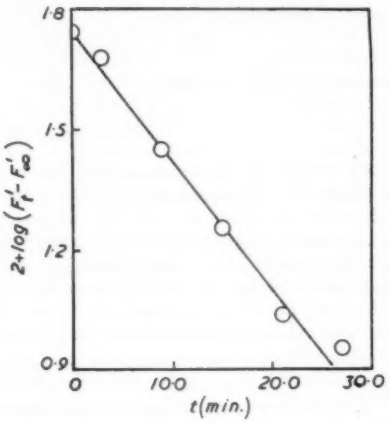


FIG. 2. *Specimen kinetic results* (Expt. 2*a*).



Results.—These are given in Tables 1—5.

TABLE 1. *Variation of the function* G *with* F′ *for hexamminocobalt*(III) *toluene*-p-*sulphonate.*

F′	G		Average G	F′	G		Average G
0·0543	0·074	0·077	0·076	0·3966	0·394	0·396	0·395
0·1127	0·166	0·173	0·170	0·5538	0·467	0·473	0·470
0·2081	0·256	0·258	0·263	0·6529	0·523	0·548	0·536
	0·263	0·267		0·7177	0·588 *	0·590 †	0·593
	0·270				0·592 †	0·598 *	
0·2858	0·328	0·336	0·332	0·7725	0·664	0·704	0·684

* Vacuum-dried immediately after acetone washing (normal procedure).
† Vacuum-dried after standing under acetone for 30 min.

TABLE 2. *Variation of the function* G *with* F′ *for oxalatotetramminocobalt*(III) *naphthalene*-2-*sulphonate.*

F′	G		Average G	F′	G		Average G	F′	G		Average G
0·1142	0·068	0·072	0·070	0·4277	0·223	0·225	0·224	0·6513	0·345	0·353	0·349
0·2252	0·133	0·145	0·139	0·4710	0·249	0·253	0·251	0·7603	0·412	0·431	0·422
0·3549	0·195	0·206	0·200								

TABLE 3. *Specimen kinetic results* (*Expt.* 2*a*): *Deuterium loss from hexamminocobalt*(III) *ion to an acetate buffer.*

[AcOH] = 0·03898M; [KOAc] = 0·08M; [KCl] = 0; $[Co(NH_3)_6Cl_3]$ = 0·00333M.
Measured pH = 4·96. Total ionic strength = 0·10M.

Time (min.)	G		Average G	F_t'	$F_t' - F_\infty'$	$2 + \log(F_t' - F_\infty')$
0·00	0·480	0·475	0·476	0·562	0·551	1·741
	0·472					
3·00	0·447	0·434	0·440	0·487	0·476	1·678
9·00	0·330	0·343	0·336	0·292	0·281	1·449
15·00	0·250	0·253	0·251	0·190	0·179	1·253
21·00	0·172	0·184	0·178	0·120	0·109	1·037
27·00	0·144	0·137	0·140	0·091	0·080	0·953
∞	—	—	—	—	0·011 (calc.)	—

The first-order character of this reaction is illustrated by the rectilinear plot of Fig. 2. The rate constant, $k = \frac{1}{t} \ln \frac{F_0' - F_\infty'}{F_t' - F_\infty'}$, was evaluated from the slope of this graph.

TABLE 4. *Summary of kinetic results with hexamminocobalt*(III) *chloride.*

[Ammine] = 0·00333M.

Expt. No.	[AcOH]	[KOAc]	[KCl]	Total ionic strength	pH	$10^4\lambda$ (sec.$^{-1}$)
		(Molarities)				
1*a*	0·01949	0·04	0·04	0·10	4·85	8·96
1*b*	0·03802	0·04	0·04	0·10	4·66	4·88
1*c*	0·06338	0·04	0·04	0·10	4·45	3·14
1*d*	0·09969	0·04	0·04	0·10	4·31	2·33
2*a*	0·03898	0·08	0·00	0·10	4·96	11·82
2*b*	0·07604	0·08	0·00	0·10	4·71	6·21
2*c*	0·1268	0·08	0·00	0·10	4·49	3·84
3*a*	0·1313	0·18	0·00	0·20	4·66	7·03
3*b*	0·4179	0·18	0·00	0·20	4·28	2·43
3*c*	0·5544	0·18	0·00	0·20	4·23	2·06
	[KH_2PO_4]	[Na_2HPO_4]				
"Phosphate"	0·0567	0·00112	0·04	0·12	5·07	9·42

TABLE 5. *Summary of kinetic results with oxalatotetramminocobalt*(III) *chloride.*

[Ammine] = 0·01M; Total ionic strength = 0·20M throughout.

Expt. No.	[AcOH]	[KOAc]	[KCl]	pH	$10^4\lambda$ (sec.$^{-1}$)	Expt. No.	[AcOH]	[KOAc]	[KCl]	pH	$10^4\lambda$ (sec.$^{-1}$)
	(Molarities)						(Molarities)				
4*a*	0·01848	0·18	0·01	5·71	3·36	5*a*	0·001451	0·02	0·17	5·95	5·46
4*b*	0·02834	0·18	0·01	5·51	1·94	5*b*	0·003053	0·02	0·17	5·39	1·47
4*c*	0·04499	0·18	0·01	5·34	1·46	5*c*	0·006259	0·02	0·17	5·12	0·83
4*d*	0·05916	0·18	0·01	5·16	1·08						

DISCUSSION

The isotopic exchange of deuterium atoms bound to tetraco-ordinated nitrogen is expected to follow a dissociative mechanism [8] in which an N–D bond is severed before the attachment of the light isotope. Such a system is one in which the exchange under heterolytic conditions would involve in the rate-determining stage the removal of D^+ from its seat of attachment, *i.e.*, a type of reaction for which the detection of general base catalysis is possible. The experiments described in this paper were directed to the study of this possibility. Associative (or additive) and synchronous mechanisms would involve co-ordination to nitrogen of more than four groups and are therefore thought to be too improbable to merit further consideration. In the following treatment it has been assumed that all N–D bonds have the same reactivity, *i.e.*, that secondary isotope effects (which would make the rupture of each N–D bond dependent on the isotopic composition at other positions) are negligible. This assumption—which is implicit in all other work on the exchange of metal ammines—is justifiable only in the sense that secondary isotope effects are of no consequence when the kinetic comparisons apply to specimens of approximately the same initial fractional abundance and to runs covering approximately the same extent of reaction. The rate constants obtained will then in each case be a comparable mean of individual rate constants. The absolute magnitude of this kind of secondary isotope effect is at present unknown.

It will therefore be convenient to represent the exchange in terms of isolated, independent N–H bonds and again to consider the system to consist of a single type of hypothetical molecule with one exchangeable hydrogen atom. The deuterium loss from the solute will then be governed by the usual first-order rate law, $-dF/dt = \lambda(F - F_\infty)$.

The absence of any perceptible exchange in acidic solutions allows us to omit from further consideration the participation of hydrogen-ion catalysis or a water-catalysed reaction and makes it unlikely that acetic acid molecules effect catalysis. If general base

[8] Gold and Satchell, *Quart. Rev.*, 1955, **9**, 51.

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catalysis operates, the velocity constant in acetic acid–acetate buffers will be composed of two additive terms corresponding to catalysis by the two bases present in solution:

$$\lambda = k_{OH^-}[OH^-]f_{OH^-}f_C/f_{X_1} + k_{OAc^-}[OAc^-]f_{OAc^-}f_C/f_{X_2} \quad . \quad . \quad . \quad (8)$$

where f_C is the activity coefficient of the complex ion and f_{X_1} and f_{X_2} those for the two transition states. Because of the known effect [9] of hexamminocobalt(III) chloride on pH, the concentration of hydroxide was not computed from the buffer composition. For every run the pH value of the solution was measured. The hydroxide-ion concentration is related to pH through the equations [10]

$$pH = -\log f_{\pm}[H^+]; \quad K_w = [H^+][OH^-]f_{H^+}f_{OH^-}$$

On the assumption that at the ionic strength used

$$f_{H^+} = f_{OH^-} = f_{\pm}$$

equation (8) becomes

$$\lambda = k_{OH^-}K_w\frac{f_C}{f_{X_1}} \times 10^{-pH} + k_{OAc^-}[OAc^-]\frac{f_{OAc^-}f_C}{f_{X_2}}$$

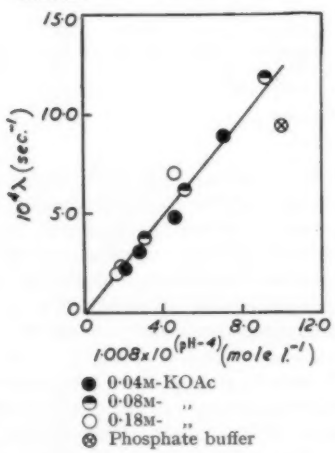

FIG. 3. pH *dependence of exchange velocity for hexamminocobalt*(III) *chloride.*

● 0·04M-KOAc
◒ 0·08M- ,,
○ 0·18M- ,,
⊗ Phosphate buffer

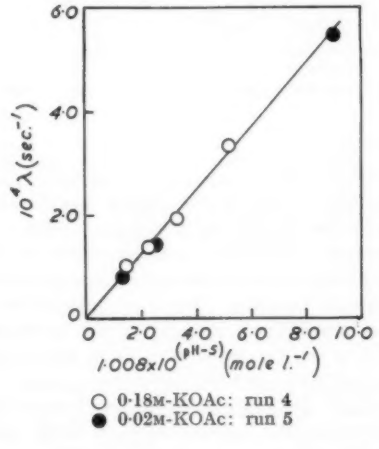

FIG. 4. pH *dependence of exchange velocity for oxalatotetramminocobalt*(III) *chloride.*

○ 0·18M-KOAc: run 4
● 0·02M-KOAc: run 5

For a series of experiments at constant acetate-ion concentration, and constant and low ionic strength

$$\lambda = k'_{OH^-}K_w \times 10^{-pH} + k'_{OAc^-}[OAc^-]$$

i.e., the experimental rate constant should be a linear function of 10^{-pH} with an intercept corresponding to the numerical value of the second term. The graphs in Figs. 3 and 4

TABLE 6. *Summary of catalytic coefficients.*

	k'_{OH^-} (sec.$^{-1}$ mole^{-1} l.)	k'_{OAc^-} (sec.$^{-1}$ mole^{-1} l.)	Maximum value of k'_{OAc^-}/k'_{OH^-}
$Co(NH_3)_6^{3+}$	$(1{\cdot}21 \pm 0{\cdot}10) \times 10^6$	$<6 \times 10^{-4}$	5×10^{-10}
$Co(NH_3)_4C_2O_4^+$	$(6{\cdot}3_4 \pm 0{\cdot}3) \times 10^4$	$<6 \times 10^{-5}$	10^{-9}

show that the intercept is indistinguishable from zero in both cases, *i.e.*, catalysis neither by acetate ion nor by water is detected. The results are summarised in Table 6.

[9] Cobb and Anderson, *Trans. Faraday Soc.*, 1944, **40**, 145.
[10] British Standard 1647: 1950.

For the results for the hexamminocobalt(III) ion the experimental points are scattered quite widely about the best straight line. The groups of points for the different series of experiments seem to show some separate trends, though none of them indicates a tendency to a finite intercept. The effect is barely outside the limits of experimental error, but it might be caused by salt effects which are expected to be considerably more important with this triply charged ion than for the univalent oxalatotetramminocobalt(III) ion.

The apparent absence of an intercept in Figs. 3 and 4 leads to the conclusion that only catalysis by hydroxide ions is operative in both reactions. The last column in Table 6 lists the maximum values which experimental uncertainties allow for the ratio k_{OAc^-}/k_{OH^-}. These values may be compared with the value of $\sim 5 \times 10^{-7}$ found for the corresponding ratio for the decomposition of nitramide,[11] where the exponent in the Brønsted catalysis law is 0·83. The absence of general catalysis can for most systems be taken to mean either that the Brønsted exponent lies close to unity—which results in experimentally inaccessible general base catalysis [12]—or that substrate and bases are involved in a rapid proton-transfer pre-equilibrium. Attention being restricted to dissociative mechanisms, the essential steps of the base-catalysed exchange are

$$XNH_2D^{z+} + B_i^- \xrightarrow{k_1} XNH_2^{(z-1)+} + B_iD \quad . \quad . \quad . \quad . \quad . \quad (9)$$

$$XNH_2^{(z-1)+} + H_2O \xrightarrow{Fast} XNH_3^{z+} + OH^- \quad . \quad . \quad . \quad . \quad . \quad (10)$$

$$B_iD + OH^- \overset{Fast}{\rightleftharpoons} B_i^- + DOH$$

where XNH_2D^{z+} stands for the heavy hexamminocobalt(III) or oxalatotetramminocobalt(III) ion and B_i^- for the catalysing base. This mechanism implies general base catalysis and requires that [8]

$$\lambda = \sum k_i[B_i^-]$$

To be compatible with our results the Brønsted exponent must then have a value near unity. The first step may or may not be composite in nature, involving first an association. For the case of hydroxide-ion catalysis this composite first step could be

$$XNH_2D^{z+} + OH^- \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} XNH_2D\cdot\cdot OH^{(z-1)+} \quad . \quad . \quad . \quad . \quad (11)$$

$$XNH_2D\cdot\cdot OH^{(z-1)+} \xrightarrow{k_2} XNH_2^{(z-1)+} + DOH$$

With the condition that $k_{-1} \gg k_1$ (which is essential to accord with the finding that the reaction is of first order with respect to hydroxide ions, and which is a reasonable one for the present system as estimated by the degree of ion association predicted from the Bjerrum model [13]), the rate constant λ is now given by $\lambda = k_1k_2[OH^-]/(k_{-1} + k_2)$. If $k_{-1} \ll k_2$ the occurrence of prior association has no experimentally detectable effect on the kinetic equation. If $k_2 \ll k_{-1}$, $\lambda = K_Ak_2[OH^-]$, where $K_A(\equiv k_1/k_{-1})$ is the association constant for the reaction

$$XNH_2D^{z+} + OH^- \rightleftharpoons [XNH_2D^{z+}\cdot\cdot OH^-]^{(z-1)+}$$

The determination of kinetic orders cannot provide any evidence concerning the rôle of this association in the reaction. That ionic association is important for these complexes (in the thermodynamic sense) is indicated, not only by calculations based on the Bjerrum theory, but also by the acidity of the salt solutions (as discussed below) and by the infrared spectra of the crystalline hexamminocobalt(III) chloride and iodide.[6] These measurements

[11] Brønsted and Pedersen, *Z. phys. Chem.*, 1923, **108**, 185.
[12] Brønsted and Wynne-Jones, *Trans. Faraday Soc.*, 1929, **25**, 59.
[13] Robinson and Stokes, "Electrolyte Solutions," Butterworths, London, 1955, Chapter 14.

show that there is much stronger bonding to chloride ions than to iodide ions. The difference is large for a crystal-field effect, and points to some form of stronger bonding, such as a " hydrogen bond." Also, the infrared spectrum does not show greater detail when the specimens are cooled to −183°, a temperature at which rotation of the ammonia ligands would be expected to be frozen. This suggests that the ligands are not in free rotation at room temperature either, but that some rotation-hindering bonding occurs. It is expected that the hydroxide ion would bond even more readily than the chloride ion.

The reaction scheme involving association may explain the high value of the Brønsted exponent which is required to account for the lack of catalysis by species other than OH^-, although there is at present insufficient information about the values of Brønsted exponents to say if such a special explanation is required. In the product $K_A k_2$ it is possible that the value k_2 would differ from base to base in a manner compatible with a lower Brønsted exponent, but that the catalysis by hydroxide ions could nevertheless swamp the catalysis by other bases because its high hydrogen-bonding power causes its value of K_A greatly to exceed that for other bases.

The observation of specific hydroxide catalysis cannot be explained by the simplest model for other cases of specific catalysis, *viz.*, the occurrence of a rapid proton-transfer pre-equilibrium followed by the slow step. In the present case this would be equivalent to assuming that reaction (9) and its reversal are rapid compared with reaction (10). Such a scheme is meaningless since the reversal of equation (9) can involve not only the heavy acid B_iD but also B_iH and, since $[B_iH] \gg [B_iD]$, this implies that the exchange velocity is governed by step (9). In other words, reaction (9) cannot be involved as a pre-equilibrium: it must be the rate-controlling step, as we have stated before. A statement by Anderson, Briscoe, and Spoor [15] to the effect that such a mechanism is possible and that the implied rapidity of the proton transfer from $Co(NH_3)_6^{3+}$ to the base water accounts for the acidity of the solutions of this ion is therefore misleading, despite the fact that it has been widely quoted and accepted.[14]

In fact, the acidity of the hexamminocobalt(III) ion is a direct consequence of the ionic association which we have discussed before. An association equilibrium (11) would cause an aqueous solution to have an acidic reaction. The equilibrium constant K_D for the dissociation

$$[Co(NH_3)_6OH]^{2+} \rightleftharpoons Co(NH_3)_6^{3+} + OH^-$$

has [15] the value 0·0138 mole $l.^{-1}$. Combining this with the value $1{\cdot}008 \times 10^{-14}$ for the ionic product of water, we obtain the acid ionisation constant for $Co(NH_3)_6^{3+}$ *via* the equilibrium

$$Co(NH_3)_6^{3+} + H_2O \rightleftharpoons [Co(NH_3)_6OH]^{2+} + H^+$$

as

$$K = \frac{[[Co(NH_3)_6OH]^{2+}][H^+]}{[Co(NH_3)_6^{3+}]} = \frac{K_w}{K_D} \approx 7 \times 10^{-11} \text{ mole } l.^{-1}$$

This value is compatible with direct pH measurements and potentiometric titrations of aqueous solutions of hexamminocobalt(III) chloride, which we have carried out to verify this point.

On this view, the hexamminocobalt(III) ion is an acid, not by virtue of its ability to act as a proton donor, but by virtue of its affinity for hydroxide ions. It is important to recognise this distinction—which is similar to that which leads to the existence of separate acidity functions [16] H_0 and J_0—if incorrect applications of Brønsted's views on the definition of acids and bases are to be avoided. The phenomenon appears to be particularly important to the consideration of acid–base catalysis by complex ions. This has hitherto

[14] Basolo in Bailar (ed.), " Chemistry of Coordination Compounds," Reinhold, New York, 1956, p. 426; Sidgwick, " Chemical Elements and their Compounds," O.U.P., London, 1950, Vol. II, p. 1399; Stranks and Wilkins, *Chem. Rev.*, 1957, **57**, 743.

[15] Caton and Prue, *J.*, 1956, 671.

[16] Gold and Hawes, *J.*, 1951, 2102.

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always been based on the implicit assumption of their behaviour as Brønsted acid–base systems, but this may clearly not always be correct.

The twenty-fold difference in reactivity between the hexamminocobalt(III) and the oxalatotetramminocobalt(III) ions is surprisingly small if one argues that the main difference between the ions is one of total electric charge. However, the situation is not so straightforward. The charge on the hexammine is distributed mainly among the ligand molecules [17] and hence the maximum charge on any ammonia group will be $+\frac{1}{2}e$. In the oxalatotetrammine the comparable charge will lie in the range $+\frac{1}{4}e$ to $+\frac{3}{4}e$, depending on the extent of ionic character which the oxalate group retains in the complex, the upper limit being applicable if the oxalate group is completely ionic and the lower one if it is totally covalent. The exchange rate would seem to indicate that the value is in fact slightly less than $+\frac{1}{4}e$.

One of us (H. B.) acknowledges the award of a postgraduate studentship by the University of London.

KING'S COLLEGE, STRAND, W.C.2. [*Received, September 25th,* 1958.]

[17] Pauling, "The Nature of the Chemical Bond," Cornell Univ. Press, Ithaca, 2nd edn., 1940, Chap. III.

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197. *Kinetics of the Thermal Decomposition of Azomethane.*

By C. STEEL and A. F. TROTMAN-DICKENSON.

The kinetics of the thermal decomposition of pure azomethane have been reinvestigated in a static system between 0·2 and 800 mm. and 229° and 321° by measuring the rate of production of nitrogen. The effect of added gases shows that the high-pressure reaction involves short chains that may be initiated and terminated at the surface of a reaction vessel. The rate constant of the homogeneous reaction fully inhibited by propene is given by:

$$\log k\ (\text{sec.}^{-1}) = (15{\cdot}7 \pm 0{\cdot}15) - (51{,}200 \pm 250/2{\cdot}303RT)$$

THE study of the thermal decomposition of azomethane played an important part in the development of modern theories of unimolecular reactions.[1,2] Most decompositions of organic compounds that were first thought to be unimolecular and to have rate constants that fell at low pressures have since been shown to be partially chain processes. They were therefore unsuitable for the experimental verification of theories of unimolecular reactions and the dependence of their rates on energy transfer. The decomposition of azomethane was still believed to be unimolecular. The investigations of this reaction are, however, unsatisfactory by modern standards. Most of the kinetic information was obtained by following the change in pressure in a static system. It was assumed that the reaction might be represented by $CH_3{\cdot}N{:}N{\cdot}CH_3 = C_2H_6 + N_2$; the observed change in pressure was in accord with this assumption. More recently, Riblett and Rubin [3] showed that the products of the decomposition are complex. Furthermore much information on the reactions of the methyl radicals initially formed in the decomposition [4] has been obtained from the photolysis of azomethane at lower temperatures.[5] Hence it is now certain that side reactions involving methyl radicals yield methane and high-boiling products. We have followed the thermal decomposition by determining the rate of formation of nitrogen because a molecule of nitrogen is probably formed each time an N–C bond is broken.

[1] Kassel, "Kinetics of Homogeneous Gas Reactions," Chemical Catalog Co., New York, 1932.
[2] Trotman-Dickenson, "Gas Kinetics," Butterworths, London, 1955.
[3] Riblett and Rubin, *J. Amer. Chem. Soc.*, 1937, **59**, 1537.
[4] Page, Pritchard, and Trotman-Dickenson, *J.*, 1953, 3878.
[5] Jones and Steacie, *J. Chem. Phys.*, 1953, **21**, 1018.

There are still only a few unimolecular reactions whose rates have been observed to depend upon the rate of energisation by collision. Only a small fraction of these can be studied in the presence of a wide range of chemically inert gases. Such studies are of value because they provide information on the relative rates of transfer of energy on collision. The isomerisation of *cyclo*propane and the decomposition of *cyclo*butane occur at such high temperatures that the number of interesting compounds that are sufficiently stable not to disturb the chemical processes is limited. The reactions of the nitrogen oxides and their derivatives often occur at low temperatures, but the reactants, products, and intermediates all react readily with most organic substances. Experiments must therefore be confined to some inorganic gases, the rare gases, and a few fluorocarbons. Studies of a greater range of additives would be very desirable. Unfortunately the present work has shown that the decomposition of azomethane, which appeared promising, is also unsatisfactory.

Experimental

Azomethane.—*sym*-Dimethylhydrazine hydrochloride was prepared by Hatt's method [6] and dissolved in excess of sodium hydroxide to yield the free base. This solution was added slowly and with constant stirring to a suspension of mercuric oxide [7] (rapid addition once led to a minor explosion). The azomethane was distilled off on a water-bath and collected in a solid carbon dioxide trap (yield 60—70%). The gas was dried (P_2O_5 and KOH), degassed, and stored at liquid-nitrogen temperature. Its purity was confirmed by gas chromatography. No evidence of *cis*- and *trans*-isomers was found although the analytical system distinguished clearly between the but-2-enes.

Other Gases.—Propene was prepared by the dehydration of propan-2-ol. *trans*-But-2-ene and *cyclo*pentane were standard samples from the National Chemical Laboratory. Carbon dioxide was obtained by evaporation of Drikold. Sulphur-free toluene was purified by partial pyrolysis and distillation as for use in kinetic studies by the carrier technique. No impurity was detected in these gases by chromatography. *cyclo*Propane contained a trace (<0·1%) of propane, and *n*-pentane 0·05% of *iso*pentane.

Apparatus.—A Pyrex reaction vessel (609 ml.) was used for most of the runs; one of 50·2 ml. was used for pressures above 100 mm. The vessels were contained in an electric furnace kept constant to ±0·1° by a gas-thermometer controller.[8] The temperatures were measured to 0·05° with a two-junction thermocouple in a well inside the reaction vessel. Both vessels were seasoned either by carrying out several preliminary decompositions of azomethane or by decomposing allyl bromide which deposits an inert carbonaceous film.

Procedure.—In experiments with azomethane alone below 100 mm., the volume of reactant was measured in a gas burette from which it was injected into the reaction vessel at the beginning of the run. At the end of the run the products were pumped through traps cooled to −196° or below. The non-condensable methane and nitrogen were circulated through an oxidising furnace (powdered CuO 98·2%, Fe_2O_3 1·8%; 610°) and through a trap system. The nitrogen was then measured in a second gas burette. Rate constants were calculated for a first-order reaction, it being assumed that the vapours behaved as ideal gases. For the runs at 170 mm., the azomethane was admitted directly from the storage bulb to the reaction vessel and measured on a mercury manometer. Above 600 mm. the azomethane was first condensed into a small storage bulb so that an ample pressure was available. When needed, gases were added to the reaction vessel after the azomethane had been injected. The total pressure was read on a butyl phthalate or mercury manometer.

Results and Discussion

Pyrolysis of Azomethane.—A series of runs at 530° and between 5 and 25 mm. showed that the rate constant for the decomposition, k_1, was independent of the amount of azomethane decomposed to nitrogen if the conversion was kept between 1 and 10%. The experiments were among the first to be carried out and the reproducibility was not as good

[6] Hatt, *Organic Syntheses*, 1936, **16**, 18.
[7] Renaud and Leitch, *Canad. J. Chem.*, 1954, **32**, 545.
[8] Taylor and Sickman, *J. Amer. Chem. Soc.*, 1932, **54**, 602.

as was subsequently achieved. Nevertheless, the point was clearly established. Thereafter all decompositions were retricted to less than 10%.

Approximately 100 successful runs were carried out, grouped round six azomethane pressures. The rate constant for the decomposition at a particular pressure was then found by a short interpolation. This procedure was followed because it proved difficult to measure an exact quantity of gas. Runs were performed at three or four different temper-

Rate constants and Arrhenius parameters for the pyrolysis of azomethane.

$(CH_3N)_2$ (mm.)	log k (290°) (sec.$^{-1}$)	log A	E (kcal. mole^{-1})	$(CH_3N)_2$ (mm.)	log k (290°) (sec.$^{-1}$)	log A	E (kcal. mole^{-1})
0·2	$\bar{5}$·19	13·12	46·2	794·3	$\bar{4}$·29	16·82	52·9
1·0	$\bar{5}$·50	13·94	47·5	Various with C_3H_6	$\bar{5}$·8	15·7	51·2
5·0	$\bar{5}$·79	15·23	50·1	Infinite [9]	$\bar{4}$·2	16·5	52·5
20·0	$\bar{4}$·01	16·03	51·6	Infinite [10]	$\bar{4}$·4	15·9	50·2
158·5	$\bar{4}$·20	16·38	52·0				

atures for each pressure. The results obtained are expressed in terms of the Arrhenius parameters determined by a least-squares treatment. They are listed in the Table together with the rate constant for a temperature lying towards the centre of each group of determinations. The reaction vessel used at the highest pressures may not have been properly seasoned: little weight should be attached to these results.

The variation of the rate constant with pressure is in reasonably good agreement with the effect reported by Ramsperger [9] and by Rice and Sickman.[10] The high-pressure Arrhenius parameters also agree well with those obtained by previous workers, as shown in the Table.

Pyrolysis of Azomethane with Added Gases.—A series of 25 runs was carried out at 288°, 281·5°, and 261·5° in which the azomethane pressure was between 0·4 and 2·8 mm. Some of the runs were for the purpose of calibration and no gas was added, but between 20 and 60 mm. of carbon dioxide was added to the majority. The presence of the carbon dioxide raised the rate constant. Its effect is conveniently expressed in terms of a constant α defined by: α = (Amount of azomethane that would have to be added to yield the observed rate constant)/(Amount of carbon dioxide added). The numerator was found by inspection of the plot of azomethane pressure against rate constant. It was found that $\alpha = 0{\cdot}20 \pm 0{\cdot}05$ and within the rather large experimental error was independent of the pressure of azomethane and carbon dioxide. This figure agrees with Rice and Sickman's.

Experiments were then carried out in which *n*-pentane and *cyclo*pentane were added. With azomethane at 0·4—0·5 mm. and the pentane between 15 and 22 mm., $\alpha = 0{\cdot}44 \pm 0{\cdot}2$. This seemed low because it was expected that a molecule of the complexity of *n*-pentane would have at least the efficiency of azomethane in energy transfer. Similar experiments were therefore tried with *trans*-but-2-ene which should have $\alpha = 1$ because its mechanical properties are almost identical with those of azomethane. Its measured efficiency was less than that of carbon dioxide. Further experiments with *n*-pentane showed that the value of α decreased at high pentane pressures and was lower at higher azomethane pressures for the same pressure of pentane. These findings could be explained if the decomposition of azomethane involves short free-radical chains that increase in importance as the pressure is raised.

Extended series of experiments were then carried out in the presence of toluene and propene. Toluene was selected because of its proved ability to stop chain reactions; propene because it is widely believed to have the same property, at least under some conditions, is readily available, and is volatile. The results, shown in Figs. 1 and 2, can be interpreted if the added gas both accelerates the reaction at low pressures by increasing the rate of energisation and reduces the rate, particularly at high pressures, by inhibiting a short chain reaction. The chain reaction becomes more important as the pressure of

[9] Ramsperger, *J. Amer. Chem. Soc.*, 1927, **49**, 912, 1495.
[10] Rice and Sickman, *J. Chem. Physics*, 1936, **4**, 239, 242.

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azomethane is increased. This is shown by the inhibition effected by propene at higher azomethane pressures. At low pressures of azomethane only the acceleration due to the added gas can been seen. Since the same limiting rate constant is obtained for all azomethane pressures with propene above about 100 mm., this rate can be identified with the rate of the initial step in the decomposition of azomethane (1). The decomposition of the

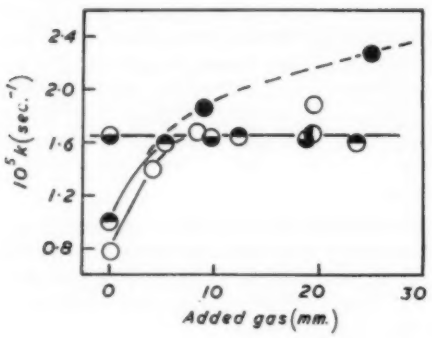

FIG. 1. *Rate constants at 276·3° for the decomposition of azomethane in the presence of toluene and carbon dioxide.*

Azomethane pressure: ○ 0·45 mm., ◓ 0·94 mm., ◐ 1·32 mm., ◒ 2·75 mm. (added gas, toluene); ● 0·94 mm. (added gas, carbon dioxide).

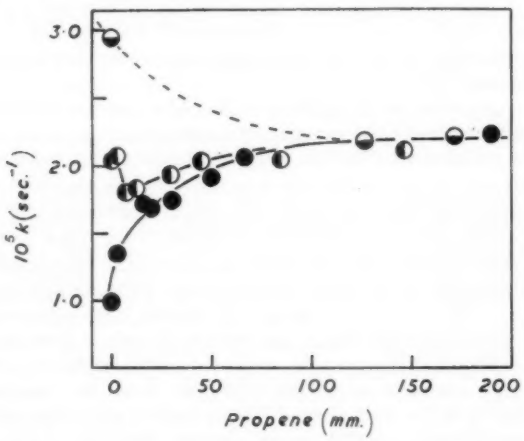

FIG. 2. *Rate constants at 276·3° for the decomposition of azomethane in the presence of propene.*

Azomethane pressure: ● 0·9 mm., ◐ 4·7 mm., ◒ 19·7 mm.

radical (2) is exothermic by some 29 kcal. mole^{-1},[4] and therefore probably occurs very rapidly. Arrhenius parameters for the fully inhibited decomposition in the presence of

$$\text{Me·N:N·Me} = \text{Me} + \text{N:NMe} \quad \ldots \quad (1)$$
$$\text{N:NMe} = \text{N}_2 + \text{Me} \quad \ldots \quad (2)$$

130—170 mm. of propene were determined with azomethane pressures of 0·93 mm. (261°, 276°, 295°, 300°), 4·7 mm. (239°, 251°, 275°, 295°), and 19·7 mm. (253°, 276°, 295°). The rate constants at all the pressures can be expressed by

$$\log k_1 \text{ (sec.}^{-1}) = (15{\cdot}7 \pm 0{\cdot}15) - (51{,}200 \pm 250/2{\cdot}303RT)$$

The standard errors are for each individual pressure. They are reduced if the results are treated as one group. The unusually high A factor is clearly established. These Arrhenius parameters are to be preferred to those of Page, Pritchard, and Trotman-Dickenson;[4] later experiments have shown that their method of injection of azomethane into the gas stream is of doubtful efficacy.

Surface Effect.—The importance of the proper seasoning of the reaction vessel to obtain reproducible results has already been stressed. The treatment is necessary because very high rates are found in clean vessels, owing either to chains starting at the walls or to a molecular reaction on the surface. When the vessels had been properly conditioned, the rate constants measured in the large reaction vessel (surface/volume = 0·85 cm.$^{-1}$) were some 1·8 times those in the small vessel (surface/volume = 2·1 cm.$^{-1}$). However, if a large excess of propene was added to the system, the rates in the large and in the small vessel were the same. At an azomethane pressure of 10 mm., the rate constant in the small vessel in the presence of 580 mm. of propene was about 1·5 times that in the absence of propene. These facts can be understood if it is supposed that chains can be ended at the wall even in seasoned reaction vessels. There are few examples of chain termination at the walls of reaction vessels except in oxidations involving molecular oxygen.

Conclusion.—Because of the complications of the decomposition that have been found in these investigations, it is not well suited to yield information on energy transfer and the behaviour of unimolecular reactions at low pressures. Furthermore, little can be said about the elementary reactions that constitute the chain. Ramsperger's conclusion that the decomposition exhibited quasi-unimolecular behaviour is, however, probably correct. The rate constant almost certainly falls off below 100 mm. owing to the restricted rate of energisation. Moreover, some of the observed decline of the activation energy below the value of 51·7 kcal. mole^{-1} is probably real. At low pressures the chains contribute little to the reaction rate. This is one of the first reactions that have been found to exhibit the decline that is predicted by the theory of unimolecular reactions.

CHEMISTRY DEPARTMENT, EDINBURGH UNIVERSITY. [*Received, October 28th,* 1958.]

[11] Taylor and Jahn, *J. Chem. Physics,* 1939, **7**, 474.

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198. *Mode of Proton Addition to Conjugated Double Bonds.*

By ALBERT WASSERMANN.

The light absorption and electrical conductance have been measured of vitamin-A acetate, a polyene with five conjugated double bonds, in benzene without and with trichloroacetic acid. The polyene is protonated in the presence of the acid; some information about the structure of the carbonium ion can be obtained.

IN previous papers [1-3] the proton transfer from trichloroacetic acid to nine conjugated polyenes has been investigated, but in most cases the structure of the resulting carbonium ions has not been specified. It is now shown that another polyene, vitamin-A acetate, containing five conjugated double bonds, accepts protons, under conditions similar to those in the earlier experiments, and that the electronic spectrum of protonated vitamin-A acetate enables one to decide whether the proton goes to the middle part of the conjugated system or to its ends.

It is assumed that the proton transfer withdraws two π electrons from the conjugated double bonds and forms a new methylenic group as in the protonation of aromatic hydrocarbons.[4]

The product from trichloroacetic acid and vitamin-A acetate, prepared as specified below, is blue and characterised by a light absorption peak at 650 mμ. That vitamin-A acetate, or the vitamin itself, can be converted into deeply coloured substances is known,

[1] Wassermann, *J.*, 1954, 4329.
[2] *Idem, J.*, 1955, 581.
[3] *Idem, J.*, 1958, 1014.
[4] See, *e.g.*, Dalinga, Mackor, and Verrijn Stuart, *Mol. Phys.*, 1958, **1**, 123, where are to be found references to earlier work.

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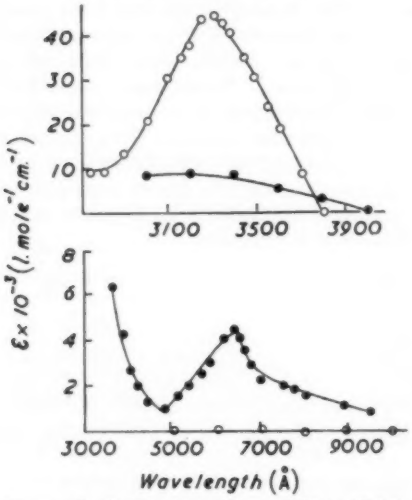
the Carr–Price reaction, for instance, having been used for the colorimetric determination of the vitamin in biological materials.[5] It is not known, however, whether the previously described coloured derivatives of vitamin-A are similar species to the carbonium-ion pairs which form the subject of this paper.

Experimental

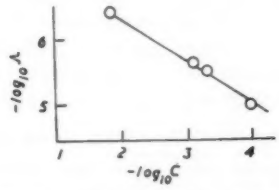
The purifications and technique have been described.[1] Vitamin-A acetate, m. p. 57°, was recrystallised from methanol. Most of the spectrophotometry was done with a special all-silica cell, of small optical path-length, 0·0944 cm., suitable for relatively concentrated solutions.

Fig. 1. *Light absorption of vitamin-A acetate in benzene solution at* 20°.



Concn. of vitamin-A acetate = $1{\cdot}84 \times 10^{-4}$ to $1{\cdot}50 \times 10^{-3}$ mole/l. ○ = No acid. ● = 0·920M-Trichloroacetic acid.

Fig. 2. *Molar electrical conductance,* Λ, *of ion pairs formed by proton transfer from trichloroacetic acid to vitamin-A acetate.*



Benzene solution, 25·0°. Ordinate: $-\log_{10}\Lambda$ (Λ in l. mole^{-1} ohm^{-1} cm.$^{-1}$); abscissa: $-\log_{10} c$ (c is concn. of ion pairs in mole l.$^{-1}$). The solution was 1·00M with respect to trichloroacetic acid.

This is important because the rate of change of the optical densities, owing to a reaction with molecular oxygen, increases with decreasing polyene concentration. Back extrapolation of optical densities and of electrical conductances to the time of mixing was carried out.[1-3] The optical densities of solutions containing protonated vitamin-A acetate depend also on the intensity of illumination, this photochemical effect probably being similar to that with other carbonium ions,[6] so all experiments were done in diffuse daylight of approximately equal intensity and the time of exposure to the light of the spectrophotometer (Unicam S.P. 500) was as short as possible.

Results.—The light absorption of vitamin-A acetate (Fig. 1) is markedly altered on addition of trichloroacetic acid, owing to proton-transfer. The equilibrium constant, K, relating to the proton uptake was obtained by plotting log K' (K' defined as in ref. 1) against trichloroacetic acid concentration and by extrapolating to zero concentration; K was so estimated to be $0{\cdot}10 \pm 0{\cdot}02$ l./mole in benzene at 20°. In these experiments the highest acid concentration was 3·96 moles/l. [here and below all concentration of trichloroacetic acid relate to the stoicheiometric molecular weight]; at about half this concentration the optical density at 6500 Å had reached its limiting value. Measurements with different polyene concentrations were carried out, and the log K' values were extrapolated in each case to $[CCl_3{\cdot}CO_2H] = 0$. The results of these

[5] See, *e.g.*, Gstirner, "Chem. Phys. Vitaminbestimmungsmethoden," Enke, Stuttgart, 1950; Moore, "Vitamin A," Elsevier, Amsterdam, 1957, chap. 7.
[6] Reid, *J. Amer. Chem. Soc.*, 1954, **76**, 3264.

tests indicated that only one acid molecule reacts with the carbon–carbon double bond of the polyene. The proton-transfer leads to electrically conducting species. In calculating specific conductances a correction was applied which took care of the small specific conductance of the acid without the polyene. The concentration of the protonated species, c, was calculated from stoicheiometric concentrations with the help of the results of the equilibrium measurements. The linear $\log \Lambda$–$\log c$ relationship (Fig. 2) is similar to that previously observed;[1-3] also the absolute values of Λ for protonated carotene, azulene, and vitamin-A acetate are of the same order of magnitude. Experiments with dioxan, which acts as a competitive proton acceptor, were carried out, as in those described by Fig. 5 in refs. 1 and 3 and by Table 2 in ref. 2. It could thus be established, as before,[1-3] that the proton transfer from trichloroacetic acid to the polyene is reversible, within an accuracy of $\pm 20\%$.

Discussion

The equilibrium measurements make it probable that only one proton is transferred to the system of five conjugated double bonds of vitamin-A acetate. A second proton may be transferred to the carbonyl oxygen of the ester grouping, but as the carbon–oxygen bond is not conjugated with the other double bonds, which are responsible for the electronic spectra here considered, protonation of oxygen need not be taken into account.

In the transfer of one proton to the carbon–carbon double bonds four pairs of mesomeric ions can be formed. Reaction with $C_{(10)}$, for instance, leads to a species the limiting resonance structures of which are shown in (I). The numbers assigned to the ten carbon atoms are the same as those in the first column of the Table, which refers also to protonated species in which the new methylenic grouping is in the other positions 2, 3,....9. One could suggest that the rate of these proton-transfers depends exclusively on the energy of the relevant transition state, which is influenced by the resonance energy, R, the π-electron localisation energy, E, or the electron density, D, of the reaction centres; and that an estimate of the R, E, or D values, which correspond to proton uptake in the 1-, 2-,....10-positions would enable one to predict the structure of the protonated species. This method is not adopted here because the dielectric constant of the solvent, benzene, is low, and therefore the proton transfer involves the whole bulky trichloroacetic acid molecule, a hydrogen-bonded dimer, rather than protons which were already dissociated before the collision with the acceptor. In this situation the relative rate of protonation may depend not only on the energy, but also on the entropy of activation, effects of the latter kind being difficult to predict in this reaction.

The structure of protonated vitamin-A acetate is deduced here with the help of a simple free-electron treatment of mesomeric ions, which is based on a knowledge of λ_1, the long-wavelength peak of the electronic spectrum and on [7]

$$\lambda_1 = (8mc/h)L^2/(N+1) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where m is the mass of the electron, c is the velocity of light, h is Planck's constant, L is the length of the chromophore, and N is the number of π electrons. Protonated polyenes are like asymmetric cyanine dyes [8,9] in that the limiting resonance structures are not identical, and therefore eqn. (1) gives merely an upper limit of λ_1. The correct expression can be obtained [7,9] if the π electrons are considered to be placed in a one-dimensional potential having a sine-curve periodicity, but in general the numerical value of the potential is not known.

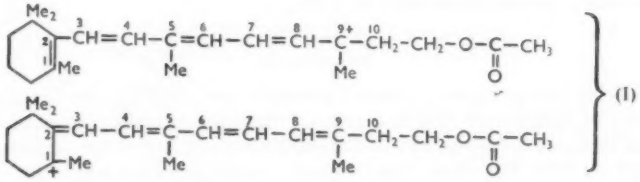
The four pairs of mesomeric vitamin-A acetate ions, referred to in the Table, are characterised by different L and N values. In order to gain information about the position of the new methylenic grouping, these parameters are estimated and introduced in (1), and

[7] Kuhn, *J. Chem. Phys.*, 1949, **17**, 1198.
[8] Brooker, *Rev. Mod. Physics*, 1942, **14**, 275. The term limiting resonance structure is used here as in ref. 6; cf. also Pauling, *Proc. Nat. Acad. Sci.*, 1939, **25**, 577.
[9] Kuhn, *Helv. Chim. Acta*, 1948, **31**, 1441; 1949, **32**, 2247; *Chimia*, 1955, **9**, 237.

the upper limit of λ_1, so obtained, is compared with the experimentally observed light absorption peak, shown in the lower part of Fig. 1 (these considerations relate to the wavelength of the peak; light-absorption intensities are not discussed here). The chromophor lengths were calculated from eqn. (2) (cf. Kuhn[7,9])

$$L = Xl_1 + 2l_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where X depends on the position of the new methylenic grouping, and l_1 and l_2 are taken to be 1·39 and 1·50 Å. These values are probably somewhat too large, but as only upper



limits of λ_1 are calculated, the conclusions are not affected. If l_2 is also taken to be 1·39 Å, λ_1 for protonation in the 1- or the 10-position becomes 3% smaller. The figures in the last

Proton taken up by carbon atom no.	No. of formal double bonds in mesomeric part of protonated species	X or N *	L (Å) *	No. of ordinary conjugated double bonds in protonated speces	$\lambda_1 \times 10^{-3}$ in Å (upper limits calc. from 1)
1 or 10	4	8	14·1	0	7·30
2 or 9	—	—	—	4	—
3 or 8	3	6	11·3	0	6·04
4 or 7	1	2	5·78	3	3·67
5 or 6	2	4	8·56	2	4·84

* These parameters relate to the mesomeric part of the protonated species.

column of the Table show that only the λ_1 value in the first line relating to 1- or 10-addition is larger than the experimental figure of 6500 Å. If the proton is transferred to the 2- or the 9-position, a mesomeric ion is not formed, the resulting carbonium ion containing four conjugated double bonds of the same type as those in the polyene before protonation. Such double bonds are also present in the species formed by 4- or 7- and 5- or 6-addition, which is indicated in col. 5 of the Table. These double bonds, in contrast to the formal double bonds in the mesomeric part of the protonated polyene, cannot give rise to light-absorption peaks above 3000 Å.[10] The experimentally determined light-absorption curve makes it probable, therefore, that the proton uptake by vitamin-A acetate leads to the mesomeric ion with the maximum number of formal double bonds.

Discussions with Professors D. P. Craig and H. Kuhn are gratefully acknowledged.

William Ramsay and Ralph Forster Laboratories,
University College, London, W.C.1. [*Received, August 19th*, 1958.]

[10] This follows, for instance, from a comparison with suitable reference substances; see *e.g.*, Naylor and Whiting, *J.*, 1955, 3037.

199. *Electronic Spectra of Conjugated Polyenes before and after Protonation.*

By Albert Wassermann.

Kuhn showed that the electronic spectra of molecules containing conjugated double bonds depend on an energy, V_0, indicating the relative importance of limiting resonance structures. In this paper V_0 for ten conjugated polyenes, before and after conversion into protonated mesomeric cations, are computed with the help of the light-absorption peaks. Numerical relationships of these V_0 values are discussed.

Previous papers [1,2,3] dealt with proton transfers of the type $A + B \rightleftharpoons C^+...D^-$, when A is trichloroacetic acid, B a conjugated polyene, and $C^+...D^-$ an ion-pair; the equilibrium constant is K, the dielectric constant of the solvent benzene and of the co-solvent A being too small to allow appreciable dissociation. The charge separation in $C^+...D^-$ could nevertheless be proved by electrical conductance measurements.

The electronic spectra of B and $C^+...D^-$ are different, but no attempt has been made to correlate the wavelength λ_1 of the light-absorption peaks with the structure of the protonated species. It is the purpose of this paper to do so by using a simple free-electron treatment developed by Kuhn.[4]

Calculation of V_0.—The π-electrons, responsible for the observed light-absorption peaks of B and $C^+...D^-$, are considered to be placed in a one-dimensional potential having a sine-curve periodicity along the chain of carbon atoms. The amplitude of the potential, V_0, a measure of the relative importance of the limiting resonance structures, can be calculated from

$$1/\lambda_1 = (V_0 - \boldsymbol{hc})(1 - 1/N) + (\boldsymbol{h}/8\boldsymbol{mc})(N + 1)/L^2 \quad . \quad . \quad . \quad . \quad (1)$$

where N is the number of π-electrons and L is the length of (Ångström units) the system of conjugated double bonds. The V_0 values of the following conjugated polyenes and of the corresponding protonated species are considered: ω-*p*-methoxyphenylpolyenealdehydes, 5-phenylpenta-2 : 4-dienal, methylbixin, and vitamin-A acetate. On protonation mesomeric cations are obtained, which are represented by the limiting resonance structures (I)—(IV) respectively. The middle parts of the formulæ (III) and (IV) have been omitted because they are obvious from the known structure of the unprotonated polyenes.[5] The mesomeric cations (I), (II), and (III) are formed by protonation of a carbonyl-oxygen atom at the end of a system of conjugated double bonds. Protonation of a carbon atom is not considered in these cases, because of the greater electronegativity of oxygen. It could be suggested that the proton is taken up by the oxygen of the methoxy-groups in (I), but this is improbable.[2] Species (IV) is formed by " end-on " addition of a proton to a system of conjugated carbon–carbon double bonds. The evidence for this mode of reaction has been given,[3] and an alternative cation specified [3] which is formed by proton transfer to the carbon atom, indicated in (IV) by an asterisk. The chromophore lengths of (IV) and of the alternative mesomeric carbonium ion are identical. These proton transfers withdraw two π-electrons from the conjugated double bonds with formation of a hydroxy- or methylenic group, which does not participate in the conjugation. The protonation is thus treated as the proton transfer to an aromatic hydrocarbon.[6]

In dealing with mesomeric ions containing benzene rings, Kuhn [4] included only one side of the benzene ring in the chromophore, as indicated by the heavy lines in (I) and (II),

[1] Wasserman, *J.*, 1958, 1014.
[2] *Idem, ibid.*, p. 3228.
[3] *Idem, ibid.*, preceding paper.
[4] Kuhn, *J. Chem. Phys.*, 1949, **17**, 1198.
[5] Cf., for instance, Zechmeister, " Carotinoide," Springer, Berlin, 1934.
[6] See footnote 4 in ref. 3.

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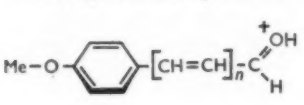
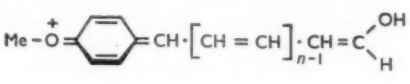
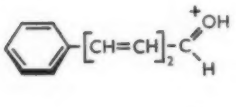
and in calculating chromophore lengths, L, he included one bond distance, l, beyond the terminal atoms forming the system of conjugated double bonds. We have adopted these conventions, all formal single and double bonds being taken as 1·46 and 1·34 Å respectively and l as 1·40 Å. The L value thus obtained was introduced into eqn. (1), together with the experimentally determined wavelengths, λ_1, and the appropriate number of π-electrons, N. The energy values, V_0, are listed in the Table. N, L, and V_0 of the protonated polyene

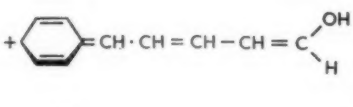


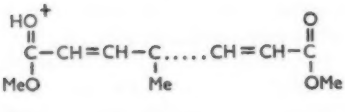
(I)



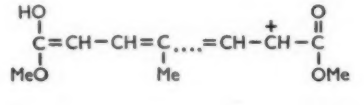


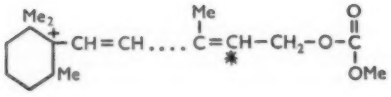
(II)



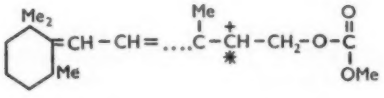


(III)





(IV)



aldehydes and of protonated methylbixin were also calculated on the assumption that the positive charge in one of the limiting resonance structures is not located on the carbonyl oxygen atom, but on the α-carbon atom. The results so obtained are not significantly different.

V_0 for conjugated polyenes before and after protonation.

Proton donor: trichloroacetic acid; solvent: benzene; temp. ~20°.

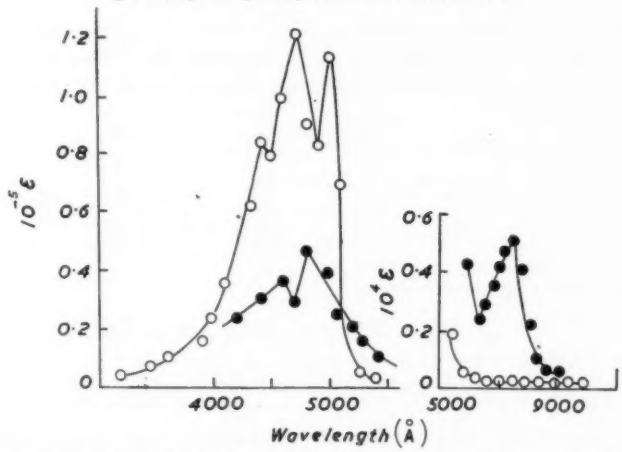
		Before protonation			After protonation		
		λ_1 (Å)	N	V_0 (kcal./mole)	λ_1 (Å)	N	V_0 (kcal./mole)
ω-*p*-Methoxyphenyl-polyenealdehyde	$n = 1$	3200	8	55·2	3450	7	43·1
	$n = 2$	3500	10	52·5	3800	9	43·2
	$n = 3$	3700	12	50·6	4100	11	41·8
	$n = 4$	4000	14	48·9	4350	13	41·0
	$n = 5$	4200	16	48·0	4500	15	41·6
	$n = 6$	4400	18	46·4	4750	17	40·2
	$n = 7$	4550	20	44·7	4850	19	40·6
5-Phenylpenta-2 : 4-dienal		3200	9	53·5	3500	8	44·5
Methylbixin		4700	21	44·5	7500	20	17·7
Vitamin-A acetate		3300	9	57·1	6500	8	5·3

Discussion.—The V_0 values of the unprotonated and protonated ω-*p*-methoxyphenyl-polyene aldehydes decrease, on the whole, with increasing n, indicating that in this homologous series, as in that previously discussed,[4] the relative contribution of one of the limiting resonance structures becomes less important if the number of conjugated double bonds is increased. Protonation produces in all cases a decrease of V_0, the variations in V_0 being smaller for unprotonated polyenes than for the protonated mesomeric cations. Thus the V_0 values in the top eight rows (right-hand column) are considerably larger than those in the last two rows of the Table; it is concluded that one of the limiting resonance structures predominates to a considerable extent in the mesomeric cations derived from the polyene aldehydes. This can be explained by a certain " localisation " of the positive charge near the electronegative carbonyl-oxygen atom. Methylbixin, in contrast to the

polyene aldehydes, contains a carbonyl oxygen at both ends of its system of conjugated double bonds and, therefore, an effect due to unsymmetrical charge localisation could be less pronounced. The V_0 value relating to protonated methylbixin is, indeed, smaller than the values in the first eight rows of the Table. The smallest V_0 value, however, is that of the protonated vitamin-A acetate. In this mesomeric carbonium ion the positive charge appears to be more evenly distributed over the chromophore than in any of the other species here considered.

Experimental.—The λ_1 values in Table 2, except those of methylbixin, were taken from previous papers.[1,2,3] The light absorption of methylbixin, m. p. 163°, recrystallised from ethanol–chloroform, before and after protonation is in the Figure. The equilibrium coefficient K relating to the proton transfer from trichloroacetic acid to methylbixin [1,7] is $0{\cdot}4 \pm 0{\cdot}1$ l./mole in benzene solution at about 20°. The equilibrium measurements make it probable that one proton only is taken up. Experiments with dioxan [1,7] showed that the protonation is reversible. For methylbixin, $-\log_{10} \Lambda$ (l. mole^{-1} ohm^{-1} cm.$^{-1}$) is 7·08 and 6·26 when

Light absorption of methylbixin in benzene at 20°.



○ without acid; ● solution 3·68M in trichloroacetic acid; methylbixin concentration $1{\cdot}00 \times 10^{-4}$ to $6{\cdot}28 \times 10^{-4}$M.

$-\log_{10} c$ [where c is the concentration of the ion pair $C^+...D^-$ (mole l.$^{-1}$) calculated from stoicheiometric concentrations and results of equilibrium measurements] is 2·72 and 3·69 respectively, at 25·0° in benzene.

Discussions with Professors D. P. Craig and H. Kuhn, and a gift of methylbixin from Dr. A. Winterstein, Hoffmann-La Roche Ltd., are gratefully acknowledged.

William Ramsay and Ralph Forster Laboratories,
University College, London, W.C.1. [*Received, November 3rd*, 1958.]

[7] Wassermann, *J.*, 1954, 4329.

200. *Electrical Conductance and Dissociation Constants of Ion-pairs formed by Proton Transfer to Conjugated Polyenes.*

By Albert Wassermann.

There is a linear logarithmic relationship between the molar electrical conductance and the concentration of ion pairs formed in benzene solution from conjugated polyenes and proton donors. The dissociation constants, K_d, of the ion pairs and limiting conductances are calculated, and a qualitative explanation for the relatively large K_d values is given.

Some electrochemical properties of ion-pairs formed by proton transfer to conjugated polyenes in benzene have been described;[1,2] there is a linear logarithmic relationship between molar electrical conductance and concentration, up to the most concentrated solutions that could be tested. These observations enable one to calculate dissociation constants, K_d, of these ion-pairs by methods now to be described. The numerical values of K_d are in accordance with conclusions derived from the electronic spectra of these polyenes.

Calculation of Dissociation Constants.—The ion-pairs $C^+ \ldots D^-$ here considered are formed by the reaction $A + B \rightleftarrows C^+ \ldots D^-$, where A is the proton donor and B is the polyene; the association constant is K', numerical values of which have been given.[1,2] The dissociation of the ion-pairs

$$C^+ \ldots D^- \rightleftarrows C^+ + D^- \quad \ldots\ldots\ldots \quad (1)$$

can be characterised by a constant, K_d, defined by

$$K_d = \frac{[C^+][D^+]}{[C^+ \ldots D^-]} \times \frac{f_{C^+} \times f_D}{f_{C^+ \ldots D^-}} \quad \ldots\ldots\ldots \quad (2)$$

The proton donor dissociates according to

$$A \rightleftarrows H^+ + D^- \text{ (equilibrium constant } K_A) \quad \ldots\ldots \quad (3)$$

where

$$K_A = \frac{[H^+][D^-]}{[A]} \times \frac{f_A + f_{D^-}}{f_A} \quad \ldots\ldots\ldots \quad (4)$$

the f's in eqns. (2) and (4) being the activity coefficients of the species indicated by the subscripts. All degrees of dissociation being assumed to be small and the activity-coefficient ratios to be unity, it can be shown that

$$K_d = \{[C^+]^2/2 + [C^+]\sqrt{([C^+]^2/4 + [A]K_A)}\}/[C^+ \ldots D^-] \quad \ldots \quad (5)$$

If it is postulated that

$$[C^+]^2/4 \gg [A]K_A \text{ and } (K_d[C^+ \ldots D^-])/4 \gg [A]K_A \quad \ldots \quad (6)$$

it follows that $[C^+] = [D^-] = K_d\sqrt{[C^+ \ldots D^-]}$, inequality (6) thus indicating that the dissociation of A is not significant compared to that of $C^+ \ldots D^-$. For the systems here considered inequality (6) is fulfilled if $K_A \ll 10^{-14}$ mole/l. This is a reasonable supposition because the constants

$$K_2 = [M^+][X^-]/[M^+X^-] \quad \ldots\ldots\ldots \quad (7)$$

relating to the dissociation of substituted ammonium salts, M^+X^-, are between 10^{-17} and 10^{-20} mole/l. in benzene solution [3,4] and it is probable that the dissociation constant of a salt is larger than that of a carboxylic acid. It is assumed, therefore, that the significant

[1] Wassermann, *J.*, 1954, 4329; 1955, 585; 1958, 1014, 3228.
[2] *Idem, ibid.*, two preceding papers; *Mol. Phys.*, 1959, in the press.
[3] Fuoss and Kraus, *J. Amer. Chem. Soc.*, 1933, **55**, 2387, 3614.
[4] Hughes, Ingold, Patai, and Pocker, *J.*, 1957, 1206.

species responsible for the conductance of the polyene salts are C^+ and D^-, formed by reaction (1). The postulated small dissociation of the proton donor A is in accordance with the observation that the specific electrical conductance of trichloroacetic acid [1] and of the other proton donors in benzene is relatively small if proton acceptors are absent; and with the results of the experiments described below in which the concentration of A was varied.

Bearing in mind the other two assumptions already mentioned, we can estimate the dissociation constant K_d, from

$$\log_{10} \Lambda = -\tfrac{1}{2} \log_{10} c + \tfrac{1}{2}(\log_{10} K_d + 2 \log_{10} \Lambda_0) \quad . \quad . \quad . \quad (8)$$

where Λ_0 is the limiting conductance of $C^+ \ldots D^-$, c is the concentration of $C^+ \ldots D^-$, and Λ is the molar electrical conductance (l. mole^{-1} ohm^{-1} cm.$^{-1}$) at concentration c. If, therefore, log Λ is plotted against log c, a straight line should result with slope $-\frac{1}{2}$ and intercept $\frac{1}{2}(\log K_d + 2 \log \Lambda_0)$.

The ion pairs here considered were prepared from the polyenes and proton donors listed in columns 2 and 3 of the Table. The linearity of the log Λ–log c relationship in the

Dissociation constants of ion pairs formed by proton transfer to conjugated polyenes in benzene at 25·0°.

No.	Polyene	Proton donor	Concn. of proton donor (mole/l.)	Range of $-\log_{10} c$ (c in (mole/l.)	No. of concns. tested	Slope of log Λ_c–log c graph	$-\log_{10} K_d$ (K_d in mole/l.)
1		$CCl_3{\cdot}CO_2H$	1·00	2—6·5	16 †	−0·57 ± 0·07	8·0 ± 0·5
2	β-Carotene *	$CHCl_2{\cdot}CO_2H$	1·00	4—7	4	−0·54 ± 0·1	8·0 ± 1·0
3		Picric acid	0·121	3—6	4	−0·60 ± 0·1	9·4 ± 1·5
4	Azulene	$CCl_3{\cdot}CO_2H$	1·00	2—5	9	0·50 ± 0·05	8·0 ± 0·5
5		$CHCl_2{\cdot}CO_2H$	1·00	4·3—5·5	3	−0·48 ± 0·10	9·8 ± 1·5
6	*p*-Methoxy cinnamaldehyde		1·00	2—5	4	−0·58 ± 0·10	12·8 ± 1·0
7	Vitamin-A acetate *	$CCl_3{\cdot}CO_2H$	1·00	2—4	4	−0·60 ± 0·10	8·8 ± 1·0
8	Lycopene *		1·00	2—6	4	−0·60 ± 0·10	8·2 ± 1·0

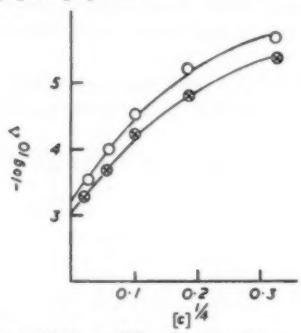
* Formulæ are given, for instance, in Zechmeister, " Carotinoide," Springer, Berlin, 1934.
† 12 concentrations are shown in Fig. 7, *J.*, 1954, 4329; 4 more concentrations were now measured.

concentration range indicated in the fifth column of the Table has already been demonstrated [1] for the systems Nos. 1—6. Similar linear relationships obtain for the systems Nos. 7 and 8, which follow from the relevant data in ref. 2. The slopes of the log Λ–log c graphs are given in the seventh column of Table 1, the deviation from the theoretical value, −0·5, being within experimental error. In order to obtain K_d from the intercepts of the log Λ–log c graphs, $-\log \Lambda_0$ is estimated by plotting $-\log_{10} \Lambda$ against $c^{\frac{1}{2}}$ and by extrapolating the resulting smooth curves to $c^{\frac{1}{2}} = 0$. Two typical plots are shown in Fig. 1. In all systems, $-\log_{10} \Lambda_0$ was 3·0 ± 0·5, except for the β-carotene–picric acid adduct, where it was 4·5 ± 1·0. $\log_{10} K_d$ of these ion-pairs is in the last column of the Table.

These dissociation constants relate to benzene–cosolvent mixtures, *e.g.*, to a benzene solution 1M with respect to trichloroacetic acid. It could be suggested that the numerical value of K_d is influenced by the cosolvent, even if eqn. (3) does not contribute a significant number of carriers of the current. Experiments were carried out, therefore, with the β-carotene–trichloroacetic acid adduct, in which the molar conductance of the ion-pairs was measured, while both the trichloroacetic acid and the ion-pair concentrations were varied. Fig. 2 shows a typical set of results relating to constant ion-pair concentration, c, and to varying acid concentrations, [A]. As log Λ is a linear function of [A], within experimental error, a linear extrapolation to $[A] \longrightarrow 0$ enables one to estimate log $\Lambda^{[A] \longrightarrow 0}$ for the specified ion-pair concentration, c. Similarly log $\Lambda^{[A] \longrightarrow 0}$ was

estimated for other c values, the results of all these measurements being shown in Fig. 3; it is a linear function of log c, the slope of the straight line being $-0{\cdot}43 \pm 0{\cdot}10$. Extrapolation of a plot of $-\log_{10}(\Lambda^{[A]\rightarrow 0})$ against $c^{\frac{1}{2}}$ to $c^{\frac{1}{2}} = 0$ indicates that $-\log(\Lambda_0^{[A]\rightarrow 0})$ is $3{\cdot}0 \pm 0{\cdot}5$, $\Lambda_0^{[A]\rightarrow 0}$ being in the same units as the other Λ_0 and Λ values. It follows therefore, from eqn. (9) and the intercept of Fig. 3, that $-\log_{10}(K_d^{[A]\rightarrow 0}) = 8{\cdot}2 \pm 0{\cdot}7$, $K_d^{[A]\rightarrow 0}$ being in mole/l. This value agrees, within the limits of the experimental errors, with $-\log K_d$ in the first row of Table 1, and it appears that the cosolvent does not alter the order of magnitude of this dissociation constant.

FIG. 1. *Calculation of limiting conductance, Λ_0, of ion-pairs formed by proton transfer to conjugated polyenes.*



Benzene solution, 25°. Proton donor = trichloroacetic acid, 1·00 mole/l. ○ = Lycopene; ⊗ = β-carotene.

FIG. 3. *Molar electrical conductance, $\Lambda^{[A]\rightarrow 0}$, of β-carotene–trichloroacetic acid adduct, $C^+ \ldots D^-$, extrapolated to zero trichloroacetic acid concentration in benzene solution at 25·0°.*

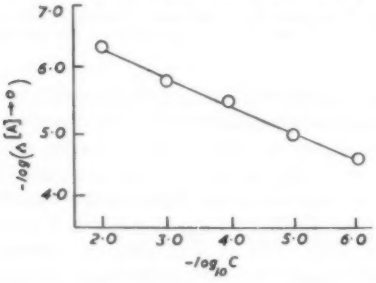
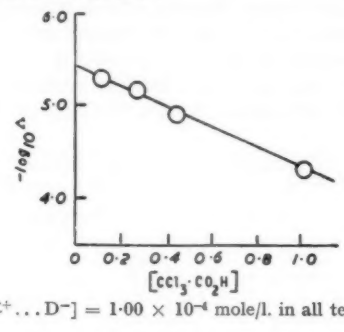
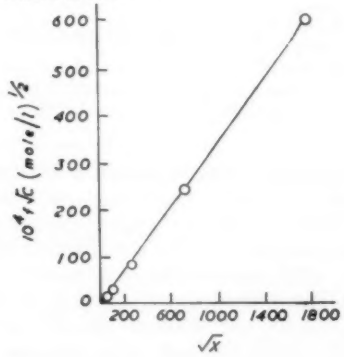


FIG. 2. *Molar electrical conductance, Λ, of β-carotene–trichloroacetic acid adduct, $C^+ \ldots D^-$, in benzene at 25·0°.*



$[C^+ \ldots D^-] = 1{\cdot}00 \times 10^{-4}$ mole/l. in all tests.

FIG. 4. *Calculation of dissociation constant of ion-pairs formed by proton transfer from trichloroacetic acid to β-carotene in benzene solution at 25·0°.*



There are two possible objections: the activity-coefficient ratio in eqn. (2) has been assumed to be unity and the estimation of Λ_0 is based on empirical extrapolation. For these reasons, $K_d^{[A]\rightarrow 0}$ for β-carotene–trichloroacetic acid has also been calculated by a convergent approximation method, described by Fuoss and Kraus,[5] in which a function $\sqrt{X} = \sqrt{[(1-\gamma)/\gamma]}$ is plotted against $f\sqrt{c}$, where γ is the degree of dissociation of an ion-pair, f is an activity coefficient, and c is the concentration of the ion-pair. Values of $\Lambda^{[A]\rightarrow 0}$ from Fig. 3, $\Lambda_0^{[A]\rightarrow 0} = 1{\cdot}0 \times 10^{-3}$ l. mole^{-1} ohm^{-1} cm.$^{-1}$, and an f value calculated as by Fuoss and Kraus [5] (with an a value, assumed to be the minimum counter-ion distance, given below) being used, Fig. 4 was obtained. The straight line passes the

[5] Fuoss and Kraus, *J. Amer. Chem. Soc.*, **1933**, **55**, 476.

origin, thereby indicating [5] that $\Lambda_0^{[A]\rightarrow 0}$ has been correctly estimated. The slope of the graph in Fig. 4, $\sqrt{K_d}^{[A]\rightarrow 0}$, is $3{\cdot}19 \times 10^{-5}$ (mole/l.)$^{\frac{1}{2}}$, which agrees, within experimental error, with the value obtained by the alternative method. This value can be used to calculate that the minimum counter-ion distance [6] is 13·2 Å.

Discussion.—It has been mentioned that the constants, K_2, of substituted ammonium salts in benzene are between 10^{-17} and 10^{-20} mole/l., while the K_d values of the polyene salts are between 10^{-6} and 10^{-13} mole/l., as shown in the last column of the Table. In the cation M^+ of the ammonium salts the positive charge must be localised on the electronegative nitrogen atom, and in most of the mesomeric polyene cations the charge is probably spread over the conjugated double bonds.[1,2] It is suggested, therefore, that the cation C^+, formed in reaction (1), is characterised by a relatively small charge density, and that this accounts for K_d being larger than K_2. The charge density of the various polyene cations, however, is not equally low: spectroscopy [2] indicates that the positive charge of the cation derived from *p*-methoxycinnamaldehyde is somewhat localised near the carbonyl oxygen. It is not surprising, therefore, that the K_d value in the sixth line of Table 1 is smaller than the dissociation constants of the other polyene adducts, although it is still larger than the K_2 values relating to the substituted ammonium salts.

The latter species are characterised by conductance minima in benzene solution,[3,4] the concentration, $c_{min.}$, being in most cases between 10^{-3} and 10^{-5}M. Fuoss and Kraus [3] showed that the minima are brought about by the formation of triple ion $\overset{+}{M}\overset{-}{X}\overset{+}{M}$ or $\overset{-}{X}\overset{+}{M}\overset{-}{X}$, the constant

$$K_3 = [\overset{+}{M}\overset{-}{X}][\overset{-}{X}]/[\overset{-}{X}\overset{+}{M}\overset{-}{X}] = [\overset{+}{M}\overset{-}{X}][\overset{-}{M}]/[\overset{+}{M}\overset{-}{X}\overset{+}{M}]$$

being approximately $c_{min.}/3$. The relatively small charge density of the polyene cation is probably responsible for K_3 being so large that $c_{min.}$ cannot be observed in the concentration range specified in the fifth column of Table 1.

Using Walden's rule,[7] Fuoss and Kraus [8] estimated that the limiting conductance of substituted ammonium salts in benzene solution at 25° is 0·1 l. mole^{-1} ohm^{-1} cm.$^{-1}$, which is about 100 times larger than the Λ_0 values of most of the polyene salts. The discrepancy may be due to the fact that the polyene cations are less symmetrical, thereby making Walden's rule, based on measurements with substituted ammonium salts, not applicable.

Experimental.—The K_d values in the Table were calculated from earlier results,[1,2] but Figs. 2—4 are from new experiments. In each run the ion-pair concentration, *c*, had to be computed from stoicheiometric concentrations, with the help of the association constants, *K'*, defined and measured as before.[1] Some new *K'* values were determined with a special silica cell of 0·1 cm. optical path length. Purification of reagents and the experimental technique have been described.[1] A few experiments, from which moisture was carefully excluded, were done as follows. A film of trichloroacetic acid, prepared by removal of solvent *in vacuo*, was dried at a pressure of less than 0·1 mm. at about 30°. It was dissolved *in vacuo* in dry benzene and filled through a greaseless tap into a conductance cell constructed for high vacuum work, a dry β-carotene solution being also added through greaseless taps. Λ so obtained agreed to within ±10% with the results of measurements in which moisture was not so carefully excluded.

William Ramsay and Ralph Forster Laboratories,
University College, London, W.C.1. [*Received, November 3rd*, 1958.]

[6] Bjerrum, *Kgl. Danske Vidensk. Selskab.*, 1926, **7**, No. 9; Fuoss and Kraus, *J. Amer. Chem. Soc.*, 1933, **55**, 1019.
[7] See Harned and Owen, "The Physical Chemistry of Electrolytic Solutions," Reinhold, New York, 1950, pages 183—186.
[8] Fuoss and Kraus, *J. Amer. Chem. Soc.*, 1933, **55**, 3618.

201. *The Reaction between Ammonia and Transition-metal Halides. Part V.* The Reaction of Ammonia with Titanium*(IV) *Bromide and Titanium*(IV) *Iodide.*

By G. W. A. Fowles and D. Nicholls.

Titanium(IV) bromide and iodide have been shown to form di- and hexa-ammoniates when ammonia is passed through their solutions in organic solvents. In liquid ammonia the halides are ammonolysed, titanium(IV) iodide being completely soluble. Ion-exchange studies indicate the formation of complex anionic species of the type $[TiX_n(NH_2)_{6-n}]^{2-}$. At −36° the compounds $TiBr_4,8NH_3$ and $TiI_4,8NH_3$ are formed, and tensimetry indicates that these are mixtures containing mainly $TiBr(NH_2)_3$ and $TiI(NH_2)_3$ respectively. On thermal decomposition, $TiBr_4,8NH_3$ gives the simple adduct $TiBr_4,2NH_3$ as a red sublimate, and a residue of TiNBr. TiN is the final product formed by the decomposition of $TiI_4,8NH_3$.

The reactions of liquid ammonia with metal halides have recently been studied in some detail. It has, for instance, been shown that titanium(IV) chloride,[1] vanadium(IV) chloride,[2] and tin(IV) chloride [3] are ammonolysed, and that when the ammonium chloride is removed by washing with liquid ammonia ammonobasic halides of formula $MCl(NH_2)_3$ are produced. Much less is known of the ammonolysis of the corresponding bromides and iodides, however, and nothing of the reaction of ammonia with titanium(IV) iodide. Work on the titanium(IV) bromide–ammonia reaction has been limited to an early investigation by Ruff and his co-workers [4,5] who obtained a compound $TiBr_4,8NH_3$, which when washed with liquid ammonia left a solid of variable composition; thermal decomposition of this product at 270° *in vacuo* gave a substance of formula TiNBr.

In view of the limitations of Ruff's study we have re-investigated the reaction of ammonia with titanium(IV) bromide, and also examined the analogous titanium(IV) iodide–ammonia reaction.

Experimental

Materials.—Titanium(IV) bromide was prepared by heating titanium metal sponge with bromine under reflux; excess of bromine was distilled off, and the titanium(IV) bromide purified by distillation *in vacuo* (Found: Ti, 13·2; Br, 86·7. Calc. for $TiBr_4$: Ti, 13·0; Br, 87·0%). Titanium(IV) iodide was prepared by heating titanium sponge and excess of iodine under reflux in carbon tetrachloride. After the removal of the excess of iodine and carbon tetrachloride, the titanium(IV) iodide was distilled *in vacuo*, the final traces of iodine being pumped off at 100° (Found: Ti, 8·85; I, 91·1. Calc. for TiI_4: Ti, 8·62; I, 91·4%). Liquid ammonia was dried over sodium. 2 : 2 : 4-Trimethylpentane was dried (P_2O_5); carbon disulphide was shaken with aqueous potassium permanganate to remove hydrogen sulphide and dried (P_2O_5). Other reagents, of "AnalaR" grade, were freed from traces of moisture by placing them in a vacuum for several hours immediately before use.

Analyses.—Nitrogen and titanium were determined as described previously.[1] Bromine was determined gravimetrically as silver bromide, and iodine by titration with potassium iodate.

Magnetic moments were measured as previously described.[6]

Reactions and tensimetry were carried out in the usual type of all-glass closed vacuum system.[1,7]

Passage of Gaseous Ammonia into Solutions of Titanium(IV) *Halides.*—Titanium(IV) bromide

* Part IV, *J.*, 1958, 1687.

[1] Fowles and Pollard, *J.*, 1953, 4128.
[2] Fowles and Nicholls, *J.*, 1958, 1687.
[3] Bannister and Fowles, *J.*, 1958, 751.
[4] Ruff and Eisner, *Ber.*, 1908, **41**, 2260.
[5] Ruff and Friedel, *Ber.*, 1912, **45**, 1364.
[6] Fowles and Pleass, *J.*, 1957, 1674.
[7] Fowles and Pollard, *J.*, 1952, 4938.

or iodide was dissolved in a suitable solvent, 2 : 2 : 4-trimethylpentane and carbon disulphide respectively, and ammonia, well diluted with dry oxygen-free nitrogen,[6] was bubbled through. With the bromide, a red compound formed initially, but complete reaction with excess of ammonia gave a yellow substance. The red compound was isolated by carrying out the reaction with excess of titanium(IV) bromide, collecting the product, and washing out the excess of bromide with 2 : 2 : 4-trimethylpentane. After being kept under the pump for 2 hr. at 30°, the red compound was analysed (Found: Ti, 12·2; Br, 77·3; N, 7·4. Calc. for $TiBr_4,2NH_3$: Ti, 11·9; Br, 79·6; N, 7·0%). By using excess of ammonia, the yellow compound was isolated and analysed (Found: Ti, 10·4; Br, 68·0; NH_3, 20·8. Calc. for $TiBr_4,6NH_3$: Ti, 10·2; Br, 68·2; NH_3, 21·7%). When the red compound was heated *in vacuo* to *ca.* 200° for 10 hr., most sublimed but a grey residue remained. The red sublimate again was the diammoniate, $TiBr_4,2NH_3$ (Found: Ti, 11·5; Br, 79·8; N, 6·75%). The grey residue gave analyses (Found: Ti, 34·1; Br, 55·2; N, 9·8%) corresponding to Ti : Br : N = 1·00 : 0·97 : 0·98.

Titanium(IV) iodide is not sufficiently soluble in trimethylpentane or any of the hydrocarbons or chlorinated hydrocarbons, and so carbon disulphide was used as a solvent. Since carbon disulphide reacts[6] with ammonia under some conditions, it was necessary to check whether this reaction would seriously affect the present results. When excess of ammonia was passed through carbon disulphide, however, only a white opalescence resulted, and even on prolonged passage of ammonia only a faint white precipitate was formed. On passage of ammonia through a solution of titanium(IV) iodide in carbon disulphide, a black precipitate formed at first, but this turned yellow with excess of ammonia. These two products were filtered off, washed with carbon disulphide, pumped for several hours, and analysed (Found, for black product: Ti, 8·13; I, 83·6; NH_3, 5·97%; Ti : I : N = 1·00 : 3·88 : 2·07. Calc. for $TiI_4,2NH_3$: Ti, 8·13; I, 86·1; NH_3, 5·77%. Found, for yellow product: Ti, 7·24; I, 75·0; NH_3, 16·0%; Ti : I : N = 1·00 : 3·91 : 6·22. Calc. for $TiI_4,6NH_3$: Ti, 7·28; I, 77·2; NH_3, 15·5%).

Ethylene glycol dimethyl ether was also a good solvent for titanium(IV) iodide, but when ammonia was passed through this solution only a pale yellow precipitate was formed.

Washing procedure for titanium(IV) *bromide.* Titanium(IV) bromide reacted initially with liquid ammonia to give a red compound, but with excess of ammonia an orange solid and a yellow solution were formed. After four or five washes with liquid ammonia (50 ml.), the filtrates were colourless, although if the orange solid was then pumped it partly dissolved in liquid ammonia to give a yellow solution. After some twenty washes with liquid ammonia, together with intermediate pumping, virtually all the solid had dissolved. The insoluble product was accordingly examined at various washing stages (on separate runs); it was pumped for several hours at 60° before analysis (see Table 1).

TABLE 1. *Insoluble product.*

	Analyses (%)			Ratios	
Run No.	Ti	Br	N	Ti : Br : N	Comments
1	18·3	54·6	23·1	1·0 : 1·8 : 4·3	12 washes; no intermediate pumping
2	22·2	47·5	25·9	1·00 : 1·28 : 3·98	12 washes; intermediate pumping twice
3	22·2	46·9	24·2	1·00 : 1·27 : 3·73	17 washes; intermediate pumping thrice
4 *	—	—	—	1·00 : 1·29 : 3·90	4 washes; no intermediate pumping

* In this run, a product $TiBr_4,6NH_3$ was first formed in the flow system, and then washed with liquid ammonia in the usual way. Ratios only are quoted for the analysis, since the product was hydrolysed *in situ*.

The solid was diamagnetic. It dissolved readily upon addition of a solution of ammonium bromide in liquid ammonia. Tensimetry of the insoluble product–ammonia system [Fig. 1(*a*)] at −36° shows the absence of free ammonium bromide; a 2-ammoniate appears to be formed.

Evaporation of all the washings left a heterogeneous mixture of yellow and white substances; after being pumped at 60° for several hours this mixture was hydrolysed *in situ* and analysed. Table 2 shows the results expressed in the form of an N : Br ratio. The soluble portion is assumed to be a mixture of ammonium bromide and an ammonobasic titanium(IV) bromide, and the N : Br ratio is obtained from the nitrogen and bromine still unaccounted for after deduction of that associated with the titanium.

[6] Sánchez and Bereau, *Anales Fis. Quim.*, 1945, **41**, 1117.

To separate this soluble compound, if possible, from the ammonium bromide, the initial reaction of titanium(IV) bromide with ammonia was carried out in the presence of excess of barium nitrate; any ammonium bromide would form the insoluble barium bromide. The

TABLE 2. *Soluble portion.*

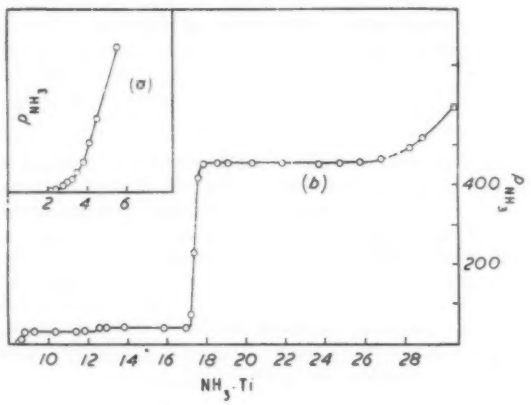
N : Br ratio, Ti being assumed to be present as:

Run No.	$Ti(NH_2)_4$	$TiBr(NH_2)_3$	$TiBr_2(NH_2)_2$	$TiBr_2(NH_2)_2,2NH_3$
1	1·00 : 1·52	1·00 : 0·96	1·00 : 0·55	1·00 : 0·92
2	1·00 : 1·86	1·00 : 1·06	1·00 : 0·61	1·00 : 1·08
3	1·00 : 2·14	1·00 : 1·04	1·00 : 0·52	1·00 : 1·08
4 *	1·00 : 1·69	1·00 : 0·93	1·00 : 0·51	1·00 : 0·90

* Initial product ($TiBr_4,6NH_3$) formed in a flow run.

whole mixture was kept at −40°, with occasional shaking, and the yellow solution was filtered from the white residue; this was washed several times with liquid ammonia to remove any soluble titanium compound. The white insoluble product was almost entirely barium bromide and contained only a negligible amount (0·10%) of titanium. The soluble product, which was

FIG. 1.



hydrolysed *in situ*, on analysis gave Ti : Br : N = 1·00 : 0·06 : 5·84; some excess of barium nitrate was also present, but this was not estimated quantitatively. Since the nitrogen was determined by distillation as ammonia from sodium hydroxide solution, the nitrate nitrogen was not estimated.

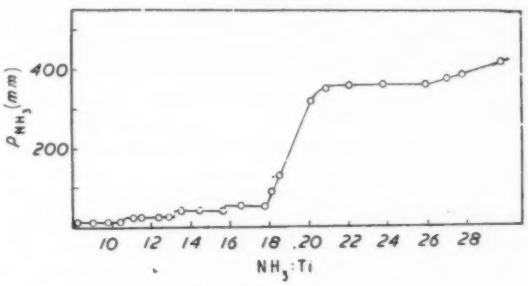
Washing procedure for titanium(IV) *iodide.* Initially titanium(IV) iodide reacted with liquid ammonia to give a greenish-black solid, but with excess of ammonia this solid dissolved completely to give a yellow solution. After evaporation of ammonia a yellow solid remained which darkened to orange-brown on pumping at 40°. The product, which was readily hydrolysed by water or dilute acids with formation of a colourless solution, was analysed (Found: Ti, 7·10; I, 75·3; N, 13·2%; Ti : I : N = 1·00 : 4·00 : 6·33. Calc. for $TiI_4,6NH_3$: Ti, 7·28; I, 77·2; N, 12·8%). In view of the colourless solution formed on hydrolysis, it seems that the titanium is still quadrivalent.

To see whether the yellow solution contained anionic titanium species, it was passed down a column of anion-exchange resin (" De Acidite FF " in Cl^- form). The 20 cm. column of resin had been prepared previously by pumping the resin dry for 24 hr. and then washing it with liquid ammonia until several successive filtrates gave an immediate blue colour with sodium metal. The column was thermostatically controlled at −40°, and the liquid ammonia solution of titanium(IV) iodide allowed to pass slowly down it. The solution emerged colourless from the column, but on evaporation of the liquid ammonia it deposited a white solid consisting entirely of ammonium chloride. On subsequent elution of the column with a solution of sodium

bromide in liquid ammonia, the eluent was found to contain titanium. It seems, therefore, that the yellow solution contains titanium in an anionic form.

Tensimetric and Thermal-decomposition Studies of the Titanium(IV) *Bromide–Ammonia and the Titanium*(IV) *Iodide–Ammonia System.*—The titanium(IV) bromide–ammonia isotherm obtained at −36° [Fig. 1(*b*)] shows the univariant portions attributable to ammonium bromide; these univariant steps have an overall length of 8·6 moles of NH_3/mole of $TiBr_4$, indicating [9] the presence of almost 3 mol. of free ammonium bromide. At −63°, the isotherm is very similar in general appearance, although the slightly shorter univariant steps (totalling 8·3 mol. of NH_3) indicate the formation of rather less ammonium bromide. In each case, the removal of excess of ammonia at the reaction temperature left a substance with overall composition $TiBr_4,8NH_3$. When this substance was heated *in vacuo*, ammonia was steadily lost (the overall composition of $TiBr_4,6NH_3$ being attained at *ca.* 60°); at 150° the product darkened to brick-red, and a bright red sublimate formed. This was resublimed (Found: Ti, 11·9; Br, 78·9;

FIG. 2.



N, 7·5. Calc. for $TiBr_4,2NH_3$: Ti, 11·9; Br, 79·6; N, 6·8%). On further heating of the product to 200°, ammonium bromide also began to sublime, leaving a brown residue, which became black at 280°. Analytical figures for various products are given in Table 3.

TABLE 3. *Involatile products formed by the thermal decomposition of* $TiBr_4,8NH_3$.

Temp.	Heating time (hr.)	Analyses (%) Ti	Br	N	Ratio Ti : Br : N	Comment
210°	2	14·6	75·6	8·35	1·00 : 3·09 : 1·95	Diamagnetic
210	18	28·1	62·0	8·90	1·00 : 1·32 : 1·08	—
280	4	32·2	56·1	9·70	1·00 : 1·04 : 1·03	—

The brown solid, obtained after short heating at 200°, dissolved completely in a small amount of liquid ammonia, although an orange solid was precipitated on dilution of the solution.

The titanium(IV) iodide–ammonia isotherm obtained at −36° (Fig. 2) shows univariant steps attributable to ammonium iodide, and the overall length of 9·9 moles of NH_3/mole of TiI_4 suggests the presence of some 2·5 mole of ammonium iodide. The product had an overall

TABLE 4. *Involatile products formed by the thermal decomposition of* $TiI_4,8NH_3$.

Temp.	Analyses (%) Ti	I	N	Ratios Ti : I : N	Comments
210°	26·2	62·2	7·70	1·00 : 0·90 : 1·00	Diamagnetic, but gives blue-green solution on hydrolysis
400	40·0	42·9	11·9	1·00 : 0·41 : 1·02	Highly pyrophoric
400	59·3	25·8	14·4	1·00 : 0·16 : 0·83	" " (Prolonged heating)

composition of $TiI_4,8NH_3$ when excess of ammonia was removed, but on heating *in vacuo* it steadily lost ammonia. Above 70°, iodine was given off, while ammonium iodide sublimed at 180° leaving a black product. The analysis of several products is given in Table 4.

[9] Bannister and Fowles, *J.*, 1958, 4374.

Discussion

In the flow runs, titanium(IV) bromide and iodide each formed a di- and a hexa-ammoniate, but there was no evidence for the formation of other products. In view of the similarity of the analogous ammoniates, it seems reasonable to consider them to have similar structures, and the arguments put forward are therefore intended to cover the products formed by both halides.

The hexa-ammoniates cannot be simple adducts, because the titanium atom is unable to assume the necessary co-ordination number of ten. It is possible, however, that the diammoniates are simple addition compounds in which the titanium(IV) halide behaves as a Lewis acid and accepts electrons from the ammonia molecules to achieve an octahedral configuration ($3d^2 4s 4p^3$). The only alternative is to consider the diammoniates as mixtures of the ammonium halide and the ammonobasic titanium(IV) halide: $NH_4X + TiX_3(NH_2)$. The sublimate which is formed by decomposing the initial product at 200° is almost certainly a simple adduct in view of its volatility and homogeneous appearance, and by analogy with the well-established volatile diammoniates of the tin(IV) halides,[3,9] and its formation is readily explained, irrespective of whether the initial diammoniate is an adduct or a mixture:

$$\left.\begin{array}{l}\text{(i) } TiBr_4.2NH_3 \longrightarrow TiBr_4 + 2NH_3 \\ \text{(ii) } TiBr_3(NH_2) + NH_4Br \longrightarrow TiBr_4 + 2NH_3\end{array}\right\} \xrightarrow[\text{surface}]{\text{on cold}} TiBr_4.2NH_3$$

Side reactions in the " hot zone " would produce the TiNBr which is also formed.

It is less certain that the original diammoniate is a simple adduct, although several observations agree with this concept. Thus, although a mixture $TiBr_3(NH_2) + NH_4Br$ has the required overall composition, the ammonobasic titanium(IV) bromide should form a strong diammoniate itself, making the overall composition that of a tetra-ammoniate. A second point is that no black product was obtained when ammonia was passed through a solution of titanium(IV) iodide in ethylene glycol dimethyl ether, even though a yellow product was formed with excess of ammonia; the ether would itself form a chelate addition compound, and it seems unlikely that ammonia would co-ordinate in preference, although ammonolysis would occur with excess of ammonia. On the whole, it is probable that the diammoniate is a simple adduct.

Since the hexa-ammoniates cannot be simple adducts, it is evident that ammonolysis has occurred with excess of ammonia, giving a mixture of ammonium halide and the corresponding ammonobasic titanium(IV) halide. On the assumption that the titanium atom has a convalency of six or less, two simple formulations are possible: (i) $TiX_2(NH_2)_2.2NH_3 + 2NH_4X$ and (ii) $TiX(NH_2)_3 + 3NH_4X$. There is no conclusive evidence in favour of either of these, and it is shown below that the washing and tensimetric experiments indicate the presence of both.

When titanium(IV) bromide reacted with excess of liquid ammonia, it mostly dissolved, although some residue (containing about 30% of the original titanium) remained even after extensive washing; the iodide, however, dissolved completely. We will consider the soluble products to be the major ones, and leave discussion of the insoluble bromide residue for the moment.

A heterogeneous solid was, for instance, obtained on evaporation of either solution, and analysis of the bromide product (cf. Table 2) showed it to be a mixture of ammonium bromide and either $TiBr(NH_2)_3$ or $TiBr_2(NH_2)_2.2NH_3$. Although the products are obviously mixtures, it is not unlikely that the solubility in liquid ammonia is caused by interaction of these constituents to form complex ions,[2] so that titanium(IV) iodide, for instance, might react with liquid ammonia according to the scheme: $TiI_4 + 6NH_3 \longrightarrow TiI(NH_2)_3 + 3NH_4I \longrightarrow [NH_4]_2[TiI_3(NH_2)_3] + NH_4I$. The ion-exchange experiments show quite conclusively that a complex titanium anion is in fact present in the iodide solution, and if we assume the titanium atom to attain a covalency of six then the anion is most likely to be

$[TiI_3(NH_2)_3]^{2-}$. (This assumes that polynuclear species are not present.) The soluble bromide product probably contains similar anions, so that when the initial reaction is carried out in the presence of barium nitrate, the bromine is displaced from the labile titanium anion by nitrate ion, and precipitated as barium bromide:

$$[TiBr_3(NH_2)_3]^{2-} \xrightarrow{NO_3^-} [Ti(NO_3)_3(NH_2)_3]^{2-} + Br^-$$

The tensimetric studies at −36° show that almost 3 mol. of ammonium bromide but only 2·5 mol. of ammonium iodide are formed in the titanium(IV) bromide– and titanium(IV) iodide–ammonium systems. A little less ammonium bromide is formed at −63°. The probable explanation of these results is that by way of the equilibrium

$$TiX_2(NH_2)_2 + NH_3 \rightleftharpoons TiX(NH_2)_3 + NH_4X$$

there is almost quantitative formation of $TiBr(NH_2)_3$ at −36° with slightly less ammonolysis at lower temperatures because of the lower ionisation of the ammonia. Titanium(IV) iodide will be less completely ammonolysed, because ammonium iodide is more soluble in liquid ammonia than is ammonium bromide, and in the tensimetric experiments very concentrated and highly acidic solutions would be formed, reversing the maximum ammonolysis attained in dilute solutions.

This explanation is more satisfactory than postulating that some ammonium iodide remains undetected because it is bound up and unable to form its characteristic ammoniates; this alternative would imply that the complex anion formed in solution partly remains in the solid state. Not only would one expect the complex to be present entirely, or not at all, but it would then be very odd that the full amount of ammonium bromide is found when the complex bromide anion should be even more stable; it is well known that the stability of anionic titanium complexes falls off in the order $F^- > Cl^- > Br^- > I^-$.

We can summarise the main reactions of the titanium(IV) halides with ammonia by saying that, with excess of ammonia, three of the titanium–halogen bonds are ammonolysed, and that some of the ammonium halide will combine with the ammonobasic titanium(IV) halide to form anionic titanium species. As the solution becomes concentrated, so the ammonolysis tends to be reversed, and at the saturation point there is a mixture of ammonobasic titanium(IV) halides. The complex titanium anions break down when the ammonia is removed, and the mixture of ammonium halide and ammonobasic titanium(IV) halides remains:

$$\begin{array}{ccccc} TiX_4 & \longrightarrow & \ldots\ TiX_2(NH_2)_2 + 2NH_4X & \overset{NH_3}{\rightleftharpoons} & TiX(NH_2)_3 + 3NH_4X \\ & & \uparrow\downarrow & & \uparrow\downarrow \\ & & [NH_4]_2[TiX_4(NH_2)_2] & \overset{NH_3}{\rightleftharpoons} & [NH_4]_3[TiX_3(NH_2)_3] + NH_4X \end{array}$$

With titanium(IV) chloride,[1] only a small amount of the reaction product dissolves in liquid ammonia, and an insoluble ammonobasic titanium(IV) chloride, $TiCl(NH_2)_3$, remains. Titanium(IV) bromide largely dissolves, however, although some solid remains, which even on exhaustive washing and pumping between washes still has a Ti : Br : N ratio of 1·0 : 1·3 : 3·7. Since the insoluble residue no longer dissolved after four or five washes unless it was first pumped, it seemed that the residue must either be a polymer, which broke down on pumping, or contain trapped titanium(IV) bromide. Some bromide might not have reacted, since the bromide used was in rather large crystals so that the centre could be protected by surface reaction products. Accordingly, the hexa-ammoniate from a flow run was washed with liquid ammonia, and in this case most of it dissolved in only a few washes without intermediate pumping to leave a residue similar to that finally obtained in straight washing runs. Since the hexa-ammoniate would not contain unchanged titanium(IV) bromide, and is unlikely to be highly polymeric (because it is formed from

solution), it seems that the pumping effect was indeed a matter of " pulling out " unchanged bromide. The final residue, however, is still high in bromine and particularly in nitrogen content, compared with that expected for $TiBr(NH_2)_3$. Ruff and Eisner,[4,5] who obtained a somewhat similar analysis, suggested a mixture of $2Ti(NH_2)_4,TiBr_4,8NH_3$ and $3Ti(NH)_2,TiBr_4,8NH_3$, and although this is clearly impossible, the non-stoicheiometric composition does imply a mixture. The main component is probably $TiBr(NH_2)_3$, which is soluble only in excess of ammonium bromide, so that the readily soluble ammonium bromide will have been washed away before all the $TiBr(NH_2)_3$ has dissolved. The other likely component is $TiBr_2(NH_2)_2,2NH_3$; on prolonged washing this will gradually become ammonolysed, producing $TiBr(NH_2)_3$ and NH_4Br, much of which will dissolve as the complex $[NH_4]_2[TiBr_3(NH_2)_3]$. The mixture of these two components required to produce the correct Ti : Br ratio will still give a low Ti : N ratio (1 : 3·3), and it is likely that $TiBr_2(NH_2)_2$ is present partly as a tetra-ammoniate, this ammonia of addition being partly lost on pumping.

These observations are in agreement with the tensimetric experiments, and the uptake of almost 2 mol. of ammonia by the insoluble residue around −36° is readily accounted for:

$$2NH_3 + TiBr(NH_2)_3 \longrightarrow TiBr(NH_2)_3,2NH_3;\ TiBr_3(NH_2)_2,2NH_3 \longrightarrow TiBr_3(NH_2)_2,4NH_3$$

A comment should be made on the tetra-ammoniate, since this gives the titanium atom a co-ordination number of eight; the same behaviour was observed with tin(IV) iodide.[9] Titanium is usually assumed to have a maximum covalency of six, even though a number of apparently octacovalent compounds have been reported.[10] It is perhaps possible that the titanium atom could attain a covalency of eight with the relatively small ammonia molecule, although more probable that the two extra ammonia molecules are held in a " secondary sphere of influence," rather like the ammoniates formed by cobaltammine-type ions.[11]

Although the products formed in the tensimetric studies are similar for both the bromide and the iodide, in that overall compositions $TiX_4,6NH_3$ remain at 60°, the subsequent thermal decompositions differ; iodine is liberated from the iodide product above 70°, and there is no sublimate of $TiI_4,2NH_3$. The decomposition of the bromide product appears to follow the scheme:

$$\begin{array}{lll} TiBr_4,8NH_3 = TiBr(NH_2)_3,2NH_3 + 3NH_4Br & & -36° \\ \downarrow (1) & & \\ TiBr_4,6NH_3 = TiBr(NH_2)_3 + 3NH_4Br & & 60° \\ \downarrow (2) & & \\ TiBr_4,2NH_3 = TiBr_3(NH_2) + NH_4Br & & 150° \\ \downarrow (3) & & \\ TiBr_4 + 2NH_3 \longrightarrow TiBr_4,2NH_3 & (4) & \end{array}$$

Some of these decompositions obviously overlap, and reaction (3) is evidently incomplete because some ammonium bromide sublimes before it can react. The residue of $TiBr_3(NH_2)$ then forms TiNBr, although, as previously mentioned, the latter compound could also arise from reaction (4). From the magnetic susceptibility and chemical properties of the product, it is clear that titanium is still quadrivalent.

The thermal decomposition of the iodide product is more complicated, once the composition $TiI_4,6NH_3$ has been attained. In view of the liberation of iodine, the formation of lower-valency titanium compounds would be expected, and this is in agreement with the formation of a blue-green solution when the unsublimed product is hydrolysed, although the diamagnetism of the product shows that the titanium atom has no unpaired electrons.

[10] Trost, *Canad. J. Chem.*, 1952, **30**, 835.
[11] Spacu and Voichesu, *Z. anorg. Chem.*, 1940, **243**, 288.

A possible explanation is that a titanium–iodine bond is thermally broken (with the liberation of iodine), followed by the formation of a titanium–titanium link. The resulting species would then have chemical properties consistent with tervalent titanium, but be diamagnetic. The final product of prolonged heating at 400° contains very little iodine, and appears to be largely a nitride of titanium. A possible decomposition scheme is:

$$TiI(NH_2)_3 + 3NH_4I[\text{or } TiI_3(NH_2)_3{,}2NH_3 + 2NH_4I] \longrightarrow TiI_3(NH_2)_2 + 2NH_4I \xrightarrow{>70^\circ}$$

$$[TiI(NH_2)_2]_2 + I_2 + 2NH_4I \xrightarrow{200^\circ} (TiINH)_n + NH_3 + 2NH_4I \xrightarrow{400^\circ} TiN$$

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THE UNIVERSITY, SOUTHAMPTON. [*Received, October 6th*, 1958.]

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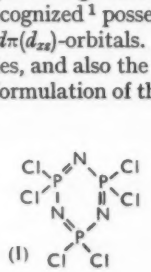
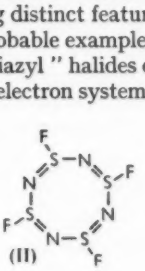
202. *Delocalization in* pπ–dπ *Bonds.*

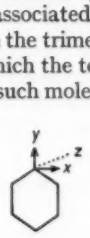
By D. P. CRAIG.

π-Electron delocalization in cyclic systems of alternating atoms A and B is discussed with reference to the contrast between examples such as borazole in which both atoms use *p*π orbitals, and the phosphonitrilic halides $(NPX_2)_n$ where it is likely that the nitrogen atom contributes a *p*π- and the phosphorus a *d*π-orbital. Certain broad differences depend upon the symmetry properties of the orbitals, supporting the idea that aromaticity is in fact of two types, the phosphonitrilic halides being the first recognized examples of the second of them. Simple molecular-orbital theory is used to examine the major points of distinction.

DELOCALIZATION in the organic aromatic compounds is associated with overlapping *p*π-orbitals on neighbouring carbon atoms. Recently another potentially aromatic situation has been recognized [1] possessing distinct features, associated with the overlapping of alternate *p*π- and *d*π(d_{xz})-orbitals. Probable examples are the trimeric (I) and tetrameric phosphonitrilic halides, and also the " thiazyl " halides of which the tetrameric fluoride (II) is illustrated. The formulation of the π-electron systems of such molecules which seems the


(I)


(II)


(III)

most likely uses *p*π-orbitals on the nitrogen atoms and *d*π-orbitals on the phosphorus or sulphur, and the same alternating pattern applies to many analogous ring systems $(AB)_n$ of first-row atoms A and second-row atoms B. In this paper the features of such plane monocyclic alternating systems will be examined by using simple molecular-orbital theory and compared with those of the familiar *p*π–*p*π aromatic compounds. They will be investigated without reference to particular compounds, the question of how far these expectations are realized in actual molecules being deferred.

Symmetry Considerations.—π-Orbitals being defined as those antisymmetric to reflection in the molecular plane there are two *d*π-orbitals, namely, d_{xz} and d_{yz}. The former have their lobes directed tangentially to the ring and the latter radially, the system of axes being that already indicated. Although these *d* orbitals are degenerate in a free atom or

[1] Craig and Paddock, *Nature*, 1958, **181**, 1052.

in a diatomic molecule they behave differently in the circumstances of our problem, as may readily be seen by symmetry analysis. Regular plane $(AB)_n$ systems belong to groups $\boldsymbol{D}_{nh}$, the cyclic order n being equal to the number of atoms of each species present. If we choose one atom of the ring and select those operations of the appropriate group which map that atom on itself we get a subgroup $\boldsymbol{C}_{2v}$ consisting of the identical operation, a two-fold rotation, and two reflections, one in the ring plane and one in a perpendicular plane containing the principal axis of symmetry. This subgroup is the same for all ring atoms in a molecule and the same for any n, and is characteristic of the atomic environment. It may be called the " site group " by analogy with a corresponding group in the theory of crystals, and with its help the types of aromatic systems can be distinguished. The π-orbital at the chosen centre must transform like an irreducible representation of this group. It is by definition antisymmetric to reflection in the ring plane and as a consequence it can belong to one of only two possible representations of the site group $\boldsymbol{C}_{2v}$. The first possibility is the one occurring in the well-known $p\pi$-orbitals which are symmetric to reflection in the perpendicular plane and antisymmetric to the two-fold rotation; and the second possibility includes antisymmetric behaviour under reflection in the perpendicular plane and symmetric behaviour under two-fold rotation. It will be observed that, while d_{yz}, like $p\pi$, belongs to the first of these representations, d_{xz} belongs to the second, defined here and throughout in terms of sets of local axes as shown. Fig. 1 illustrates the d_{xz} and $p\pi$ types schematically in a projection perpendicular to the ring plane.

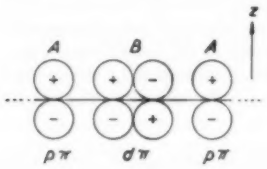


FIG. 1. *$p\pi$-Orbitals at the two centres* A *and a d_{xz} orbital at* B *shown in projection normal to the ring plane. The d_{yz} orbital is obtained from d_{xz} by a* 90° *turn about the z axis.*

The site symmetries restrict the symmetry species of the possible one-electron molecular orbitals. It is convenient to consider separately the symmetry-adapted combinations of the n atomic orbitals at A centres and those at B, leaving the question of how they combine together to form molecular orbitals for the system of A and B together. Table 1 lists the molecular orbital species which can occur in relation to the site species for $n = 3$ and $n = 4$ (six- and eight-membered rings), these being representative of the odd and the even classes,

TABLE 1. *Symmetry species of atomic orbital combinations in plane* $(AB)_n$ *molecules.*

	$n = 3$ $(\boldsymbol{D}_{3h})$		$n = 4$ $(\boldsymbol{D}_{4h})$	
l	$p\pi$ and d_{yz} *	d_{xz} †	$p\pi$ and d_{yz} *	d_{xz} †
0	a_2''	a_1''	a_{2u}	a_{1u}
±1	e''	e''	e_g	e_g
2	—	—	b_{2u}	b_{1u}

* Site species b_1. † Site species b_2.

and moreover being the most important practically. The specifying symbol l in the left-hand column of the Table is the ring quantum number to be explained in the next section. The Table shows that for both values of n the combinations may transform differently for different species of atomic orbital and, as will be shown, this leads to a significant cleavage between molecules in which A and B use orbitals of the same site species (homomorphic aromatic) and others (heteromorphic aromatic).

Molecular-orbital Energy Calculations.—The forms of the proper linear combinations of atomic orbitals in cyclic systems are determined by symmetry. We give the atoms of species A indices p running from 1 to n, denote the π orbitals by A_p, and fix their relative signs by supposing each to be generated from A_1 by successive n-fold rotations. The

orbitals at B are then denoted by $B_{p+1/2}$. The proper combinations are as follows, defined with the aid of a ring quantum number l:

$$\left.\begin{aligned}\phi_A{}^l &= n^{-1/2}\sum_p \exp(2\pi i l p/n)\,.\,A_p \\ \phi_B{}^l &= n^{-1/2}\sum_p \exp\{(2\pi i l)(p+1/2)/n\}\,.\,B_{p+1/2}\end{aligned}\right\} \quad . \quad . \quad . \quad . \quad . \quad (1)$$

These combinations have the symmetry properties listed in Table 1.

As usual, molecular orbitals are found by combining functions (1) of the same l to give stationary values of the energy. If the orbitals at A and B are identical $p\pi$-orbitals our problem is that of the monocyclic aromatic hydrocarbons, and the energies and molecular orbitals may be found from the roots of the secular equation:

$$\begin{vmatrix}\alpha-\varepsilon & 2\beta\cos(\pi l/n) \\ 2\beta\cos(\pi l/n) & \alpha-\varepsilon\end{vmatrix} = 0 \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where α and β have the meanings usual in simple molecular-orbital calculations, namely, coulomb and resonance integrals, respectively. The roots $\varepsilon_l = \alpha \pm 2\beta\cos(\pi l/n)$ are the well-known hydrocarbon molecular-orbital energies which can of course be found directly by using the higher symmetry appropriate to a molecule in which A and B are identical. If the orbitals are both of $p\pi$-type, but one is more electronegative than the other by an amount which may be expressed as ρ times the resonance integral β (as in 1 : 3 : 5-triazine, where A is carbon and B nitrogen), the secular equation is derived from (2) by putting $\alpha + \rho\beta - \varepsilon$ for the diagonal entry referring to the more electronegative atom. We find that, for all values of ρ, equation (2) leads to orbital energies which are least for $l = 0$, β being a negative quantity. The situation is no different if one of the orbit types is d_{yz} because according to the Table a d_{yz} orbital in the site group has the same symmetry behaviour as $p\pi$, and the secular equation is of the form of (2) with appropriate allowance for the different electronegativities.

Where A and B provide π-orbitals of different site symmetries, one d_{xz} and the other $p\pi$, we may take B to be the $p\pi$ centre and again write for the coulomb integral $\alpha_B = \alpha_A + \rho\beta$, allowing the parameter ρ to vary according to the different electronegativities of the orbitals. The Table shows that the orbitals $l = 0$ belong to different species and cannot interact. Accordingly the energies ε_0 must be α_A and $\alpha_A + \rho\beta$. For other values of l the secular equation must be solved:

$$\begin{vmatrix}\alpha_A-\varepsilon & 2i\beta\sin(\pi l/n) \\ -2i\beta\sin(\pi l/n) & \alpha_A+\rho\beta-\varepsilon\end{vmatrix} = 0 \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

The appearance of the sine in the off-diagonal element of (3) leads to important differences from the normal aromatic secular equation (2). First, the most stable orbital is that for $l = n/2$ or $(n-1)/2$ for n even or odd instead of $l = 0$; and, secondly, the energies of the molecular orbitals are either different from the normal aromatic case (odd n) or the same in magnitude but inverted with respect to their associated l values (even n). Typical energy level schemes are illustrated in Fig. 2.

Proceeding conventionally we may exhibit the features of the systems in a convenient way by assigning electrons to the orbitals and calculating the total energy and from it the delocalization energy per electron. We consider six- and eight-membered rings for $p\pi$–$p\pi$ and $p\pi$–d_{xz} systems and allow the electronegativity difference between atoms A and B to vary between zero and 2β. The results are shown in Fig. 3.

There are three types of behaviour. The centre curve applies to eight-membered ring systems of both aromatic types. The top curve, recording larger values of delocalization energy per electron, applies to $p\pi$–$p\pi$ six-membered rings and the lower curve, with smaller delocalization energy values, to $p\pi$–$d\pi$ six-membered rings. When A and B are equally

electronegative the conditions are those of the aromatic hydrocarbons and, as is well known, benzene has a substantially more stable π-electron system than a hypothetical planar *cyclo*octatetraene would have, a situation which is aggravated in the actual molecule by strain in the σ-bonds. However, in the $p\pi$–$d\pi$ case the eight-membered ring has a more stable π-system than the six-membered ring, so that even allowing that σ-bond strain is

FIG. 2. *π-Electron energy level patterns for* $(AB)_n$ *regular plane rings. The upper diagram refers to* $n = 3$ *and the lower to* $n = 4$. *The labels are the l values used in equation* (1). *The energy scale is in units of the resonance integral appropriate to each case and may be expected to vary, in absolute terms, from case to case.*

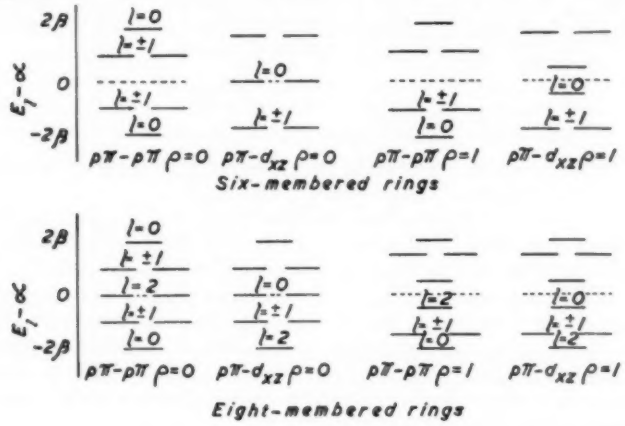


FIG. 3.

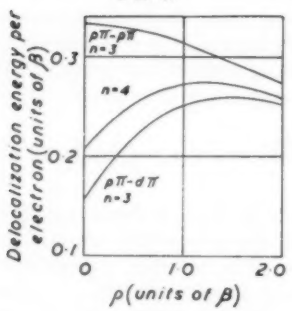
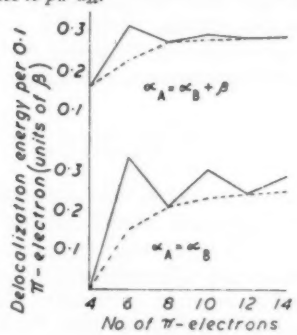


FIG. 4. *Delocalization energies per π-electron in plane* $(AB)_n$ *systems as a function of n. Upper diagram: coulomb integrals differing by* β; *lower diagram: equal coulomb parameters. Full lines refer to* $p\pi$–$p\pi$ *and broken lines to* $p\pi$–d_{xz}.



greater for the larger ring we might expect six- and eight-rings to be of comparable stability under conditions of equally electronegative atoms A and B. These features persist qualitatively when the electronegativities are allowed to differ. The three curves all tend to zero at larger values of ρ, because the π-electrons then tend to be localized on the more electronegative centre, but in approaching the common limit the curves do not cross, so that delocalization, if it occurs at all, follows a fundamentally different pattern according to whether it is of the $p\pi$–$p\pi$ or $p\pi$–d_{xz} type.

Another useful way of bringing out the difference is to compare behaviour of the

π-systems as a function of ring size, again overlooking problems connected with strain. Fig. 4 illustrates the delocalization energies per π-electron calculated from equations (2) and (3) for values of n from 2 to 7 for two cases: for equally electronegative atoms A and B, and for electronegativities differing by one unit of the resonance integral β.

The curves for $p\pi$–$p\pi$ delocalization illustrate Hückel's rule that special stability occurs in systems of $4n + 2$, not of $4n$, electrons, a result which holds even when the atoms are dissimilar. In $p\pi$–d_{xz} delocalization the variation with n is smooth, showing no equivalent of Hückel's rule, and leading in the limit of large rings to the same energy per π-electron as in the $p\pi$–$p\pi$ type.

It is clear that the primary distinction lies in the symmetry restrictions which different atomic orbitals place on delocalization, and a simple theory such as the molecular-orbital considerations used in this paper cannot be expected to do much more than to give formalized expression to the symmetry arguments. To make even semi-quantitative deductions from the results in the Figures we should note that the common unit β, as well as being different in absolute magnitude in the two cases, is also a function of the electronegativity parameter ρ: to be sure, it is easy to show that it varies only slowly in the range of ρ plotted, but comparisons should ideally be confined to particular ρ values.

Refinements to the theory described must of course include the possibility that the second-row element uses π-orbitals of both types in one and the same molecule as discussed elsewhere.[2] Refinements can more usefully be taken up in relation to the performance of the theory in particular examples which will be examined in a later paper.

Conclusions.—Some conclusions from this discussion, applying to plane cyclic arrangements of the atoms, are the following:

(i) In plane systems of alternating atoms A and B each providing one π-electron there are only two symmetry-distinguishable types of delocalization, represented as examples by neighbour $p\pi$–$p\pi$ interactions and $p\pi$–d_{xz}, the former being the type familiar in aromatic hydrocarbons and the latter not hitherto recognized.

(ii) In the familiar type of aromaticity the sextet is of dominating importance. The lower stability of π-electrons in a four- or an eight-membered ring than in a six-membered ring is well known in its relation to the *cyclo*butadiene–benzene–*cyclo*octatetraene problem.

(iii) In $p\pi$–d_{xz} delocalization the dominance of the sextet is lost. The delocalization energy per electron increases steadily with the number of π-electrons, leading to the expectation that on the basis of π-electrons alone an eight-membered ring would be more stable than a six-membered one. It can be shown that the energy per electron increases to a limiting value with increasing ring size, so that still larger rings are feasible, insofar as σ-bond strain permits them.

Finally, anticipating application to particular molecules, we note that in case the ring is non-planar conditions of π-bonding are differently affected in the two cases. A $2p_z$ orbital of a first-row element has its orientation fixed relative to the σ-bonds: that is, its axis of symmetry, the z-axis, is always normal to the plane of the three σ-bonds, leading to a rapid loss of overlapping power with at least one of its neighbours as the ring puckers. In the actual configuration of *cyclo*octatetraene, for example, each π-orbital overlaps effectively with one neighbour only, its axis being approximately perpendicular to that of the other neighbour. A $d\pi$ orbital of P or S in compounds such as (I) and (II) is in a higher quantum level than the σ-valence shell and its axis of quantization is not so rigidly fixed but may accommodate itself to give the best compromise binding with its two neighbours. Generally speaking this means that $p\pi$–$d\pi$ binding is less sensitive to non-planarity, and also that the particular distortion from the plane which is energetically favoured may not be the same as in the $p\pi$–$p\pi$ analogue.

SIR WILLIAM RAMSAY AND RALPH FORSTER LABORATORIES,
UNIVERSITY COLLEGE, LONDON.

[*Received, October 2nd,* 1958.]

[2] Craig, *Chem. Soc. Special Publ.*, 1958, No. 12, p. 343.

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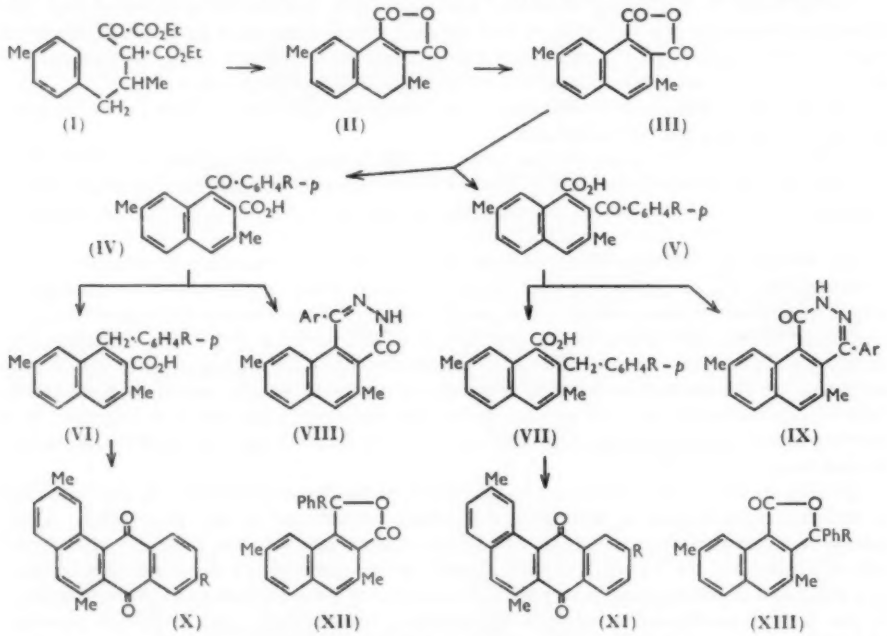
203. β-*Aroylpropionic Acids. Part IX.* Their Conversion into 1 : 2-Benzanthraquinones.*

By F. G. Baddar, Ibrahim M. Dwidar, and Munir Gindy.

The ester (I) is cyclised with 75% v/v sulphuric acid to 3 : 4-dihydro-3 : 7-dimethylnaphthalene-1 : 2-dicarboxylic anhydride, which is then dehydrogenated to 3 : 7-dimethylnaphthalene-1 : 2-dicarboxylic anhydride. The latter with arylmagnesium halides gives a mixture of 1- and 2-aroyl-3 : 7-dimethyl-2- and -1-naphthoic acid. These are separated and reduced to the corresponding benzylnaphthoic acids, which are cyclised and then oxidised to 1 : 2-benzanthraquinones.

Ethyl β-methyl-γ-*p*-tolylbutyrate [1] was condensed with ethyl oxalate in presence of potassium ethoxide to give the ethoxalyl ester [2] (I), which was cyclised and then dehydrogenated to 3 : 7-dimethylnaphthalene-1 : 2-dicarboxylic anhydride [2] (III). Interaction of this anhydride with phenyl- or *p*-methoxyphenyl-magnesium halide gave a mixture of the aroyl-acids (IV and V; R = H or MeO), the former predominating.



The structure of the acid (IV; R = H) was based on the following facts: (1) On fusion with alkali [3] it gave 3 : 7-dimethyl-2-naphthoic [4] and benzoic acid. (2) It was decarboxylated to 1-benzoyl-3 : 7-dimethylnaphthalene, which on fusion with alkali gave 3 : 7-dimethyl-1-naphthoic acid, 3 : 7-dimethylnaphthalene, and benzoic acid. 3 : 7-Dimethyl-1-naphthoic acid was obtained by refluxing the oxalyl derivative (I) with 30% sulphuric acid and dehydrogenating the product.[2]

* Part VIII, *J.*, 1957, 1699.

[1] Mayer and Stamm, *Ber.*, 1923, **56**, 1424.
[2] Cf. Baddar and Warren, *J.*, 1939, 944.
[3] Cf. Waldmann, *J. prakt. Chem.*, 1930, **127**, 195.
[4] Cf. Coulson, *J.*, 1934, 1406.

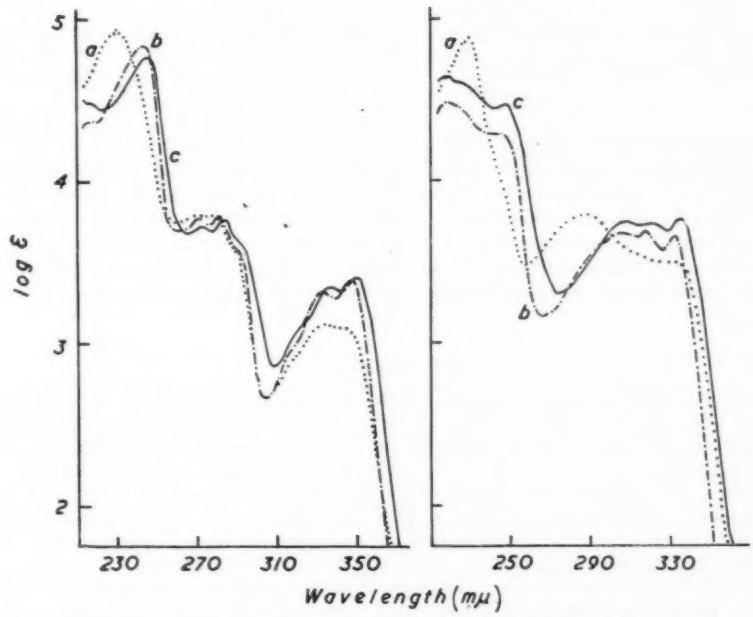
The structure of the isomeric acid (V; R = H) was established as follows: it gave on alkali fission [5] 3 : 7-dimethyl-1-naphthoic acid and benzoic acid; and it was decarboxylated to 2-benzoyl-3 : 7-dimethylnaphthalene, which was cleaved by alkali to 3 : 7-dimethylnaphthalene, benzoic acid, and 3 : 7-dimethyl-2-naphthoic acid.

Attempts to cyclise the keto-acids (IV and V; R = H) directly were not successful. They were, therefore, reduced with hydrazine hydrate in presence of sodium glycollate and ethylene glycol to the benzyl derivatives (VI and VII; R = H). Each reaction mixture contained also a neutral nitrogenous substance, probably the phthalazines (VIII and IX; Ar = Ph).

The benzylnaphthoic acids (VI and VII; R = H) were cyclised with concentrated sulphuric acid to the corresponding 1 : 2-benzanthrones, which were directly oxidised with sodium dichromate to 2′ : 4-dimethyl-1 : 2-benzanthraquinone (X = XI; R = H).

FIG. 1. *Absorption spectra of* (*a*) **3 : 7-dimethyl-2-naphthoic acid and compounds** (*b*) (XII; R = H) *and* (*c*) (XII; R = Ph).

FIG. 2. *Absorption spectra of* (*a*) **3 : 7-dimethyl-1-naphthoic acid and compounds** (*b*) (XIII; R = H) *and* (*c*) (XIII; R = Ph).



The measurements were made on a Beckman DU spectrophotometer kindly made available by NAMRO 3, *Cairo.*

The structure of the keto-acid (IV; R = OMe) was deduced from the fact that on alkali fission it gave 3 : 7-dimethyl-2-naphthoic and *p*-hydroxybenzoic acid. The isomeric acid (V; R = OMe), when similarly treated, was not cleaved but only demethylated. These keto-acids were reduced by zinc dust and alkali to the benzyl acids (VI and VII; R = OMe), which were cyclised and then oxidised to the benzanthraquinones (X and XI; R = OMe).

When the keto-acids (IV and V; R = H) were reduced with zinc amalgam and hydrochloric acid, or with zinc dust and alkali, they gave lactones (XII and XIII; R = H). The infrared spectrum of the former lactone included the characteristic stretching

[5] Cf. Braun, Manz, and Reinsch, *Annalen*, 1929, **468**, 277.

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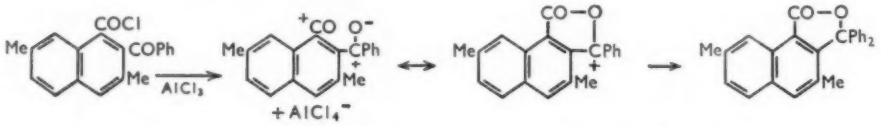
frequency for αβ-unsaturated γ-lactones [6] (1760—1740 cm.$^{-1}$). The absorption spectra of the two lactones (Figs. 1*b* and 2*b*) were identical with those of the corresponding 2- and 1-naphthoic acids (Figs. 1*a* and 2*a*).

When the acid chlorides of the keto-acids (IV and V; R = H) were condensed with benzene in presence of aluminium chloride, they did not give rise to 1 : 2-dibenzoyl-3 : 7-dimethylnaphthalene, but to the diphenyl lactones (XII and XIII; R = Ph). The same lactones were obtained by the action of phenylmagnesium bromide on the keto-acids. The structure of the former lactone follows because it has no ketonic properties and its infrared spectrum is very similar to that of the lactone (XII; R = H), showing the characteristic stretching frequency for αβ-unsaturated γ-lactones. In addition, the ultraviolet spectra of the two lactones (Figs. 1*c* and 2*c*) were identical with those of the lactones (XII and XIII; R = H) and with those of the corresponding 2- and 1-naphthoic acids, respectively. When these lactones (R = Ph) were cleaved with alkali they gave benzoic acid with 3 : 7-dimethyl-2- and -1-naphthoic acid, respectively (cf. the alkali fission of diarylphthalides [7]).



The formation of the lactone (XIII; R = Ph) from 2-benzoyl-3 : 7-dimethyl-1-naphthoyl chloride could be explained according to the annexed scheme.[8] The formation of the keto-acid (IV; R = H or OMe) in a greater proportion than (V; R = H or OMe) may be attributed to deactivation of the 2-carbonyl group towards Grignard reagents either by the electron-repelling character or the bulk of the neighbouring methyl group. The direction of alkali fission of the benzoylnaphthoic acids and benzoylnaphthalenes appears to be governed by the electron density at the carbon atoms attached to the carbonyl group.[9]

Experimental

α- *and* β-*Methyl-γ-oxo-γ*-p-*tolylbutyric Acid.*—A cold stirred mixture of methylsuccinic anhydride (30 g., 1 mol.), toluene (40 g., 1·6 mol.), and acetylene tetrachloride (100 g.) was treated portion-wise with aluminium chloride (50 g., 1·4 mol.) at <5°, stirred for 3 hr. at <5°, then for further 3 hr. at room temperature and for 4 hr. at 60—70°, left overnight, and worked up as usual. The product was crystallised from the least amount of acetic acid, to give α-methyl-γ-oxo-γ-*p*-tolylbutyric acid, m. p. 170—171° (33%). The mother-liquor was evaporated to dryness, and the oily residue crystallised from benzene–light petroleum (b. p. 50—60°) to give the β-methyl acid, m. p. 65—66° (54%) (cf. Mayer and Stamm [1]).

Ethyl β-*Methyl-γ*-p-*tolylbutyrate.*—The above β-methyl-γ-keto-acid was reduced by Martin's method to β-methyl-γ-*p*-tolylbutyric acid, b. p. 160—161°/9 mm., in 89% yield. The ethyl ester, b. p. 130—131°/7 mm., was obtained in 94% yield.

3 : 4-*Dihydro*-3 : 7-*dimethylnaphthalene*-1 : 2-*dicarboxylic Acid* (II).—A stirred suspension of powdered potassium (2 g., 1·15 atom-equiv.) in dry ether (100 ml.) was treated with absolute ethanol (2·4 g., 1·15 mol.); when hydrogen ceased to be evolved, freshly distilled ethyl oxalate (12 g., 1·8 mol.) was added in one portion. The mixture was stirred for ½ hr., then treated with ethyl β-methyl-γ-*p*-tolylbutyrate, left for 3 days with occasional stirring, and then worked up as usual.[2] The crude ethoxalyl derivative was stirred with 75% (v/v) sulphuric acid (50 ml.) at 60—70° for 1·5 hr., then poured into ice-cold water. The solid product was extracted with boiling 10% sodium hydroxide solution, and the insoluble fraction filtered off and identified as

[6] Bellamy, "The Infra-red Spectra of Organic Compounds," Methuen and Co., Ltd., London, 1956, p. 159.
[7] Hubacher, *J. Amer. Chem. Soc.*, 1944, **66**, 255.
[8] Burton and Munday, *J.*, 1957, 1727; Baddeley, *Quart. Rev.*, 1954, **8**, 371.
[9] Baddar and Gindy, *J.*, 1944, 450; 1948, 1231.

3 : 7-dimethyl-1-tetralone [10] (1·5 g.), m. p. and mixed m. p. 51°. The acid precipitated on the acidification of the alkaline solution crystallised (charcoal) from alcohol–benzene, to give 3 : 4-*dihydro*-3 : 7-*dimethylnaphthalene*-1 : 2-*dicarboxylic acid*, m. p. 190—191° (gas evolution), in 75% yield (Found: C, 67·9; H, 5·5. $C_{14}H_{14}O_4$ requires C, 68·3; H, 5·7%). Larger batches gave a lower yield.

The *anhydride* was obtained in 81% yield by heating the acid (6·8 g.) with acetyl chloride (30 ml.) for 1 hr. Crystallised from light petroleum (b. p. 50—60°), it had m. p. 119—120° (Found: C, 74·1; H, 5·3. $C_{14}H_{12}O_3$ requires C, 73·7; H, 5·3%).

The dimethyl ester obtained (72%) from the acid and diazomethane was an oil, b. p. 165—170°/5 mm.

3 : 7-*Dimethylnaphthalene*-1 : 2-*dicarboxylic Anhydride* (III).—The above dihydro-anhydride (2·8 g.) was heated with sulphur (0·8 g.) at 210—215° for 1 hr., then worked up as usual. Crystallisation from benzene gave 3 : 7-*dimethylnaphthalene*-1 : 2-*dicarboxylic anhydride* (91%) as needles, m. p. 225—226° (Found: C, 74·2; H, 4·7. $C_{14}H_{10}O_3$ requires C, 74·3; H, 4·4%). The dehydrogenation was also effected by heating the dihydro-anhydride at 260—270° for 6 hr., or by exposing its benzene solution to sunlight (July) for 30 days.

Dimethyl 3 : 7-*dimethylnaphthalene*-1 : 2-*dicarboxylate*, prepared by heating the dihydro-ester with sulphur as above, had m. p. 113—114° [from light petroleum (b. p. 60—70°)] (Found: C, 71·0; H, 6·2. $C_{16}H_{16}O_4$ requires C, 70·6; H, 5·9%).

3 : 4-*Dihydro*-3 : 7-*dimethyl*-1-*naphthoic Acid*.—The crude ethoxalyl derivative (I) (19 g.) was refluxed with 30% (v/v) sulphuric acid (70 ml.) for 30 hr.,[2] the solution being allowed to evaporate to 75% of its volume during the last 6 hr. The product was extracted with sodium carbonate solution, and the neutral fraction was crystallised from light petroleum (b. p. 60—70°) to give 3 : 4-dihydro-3 : 7-dimethylnaphthalene-1 : 2-dicarboxylic anhydride (0·5 g.). The acid product was heated in a vacuum; the fraction which boiled at 160—161°/9 mm. and proved to be β-methyl-γ-*p*-tolylbutyric acid, was rejected. The residue was dissolved in sodium carbonate solution (charçoal), reprecipitated, and crystallised from light petroleum (b. p. 50—60°) to give 3 : 4-*dihydro*-3 : 7-*dimethyl*-1-*naphthoic acid* (2·2 g.), m. p. 114—115° (Found: C, 77·3; H, 6·9. $C_{13}H_{14}O_2$ requires C, 77·2; H, 7·0%).

3 : 7-*Dimethyl*-1-*naphthoic Acid*.—Dehydrogenation of the dihydro-acid was carried out with sulphur as mentioned above. Crystallisation from benzene–light petroleum (b. p. 50—60°) gave 3 : 7-*dimethyl*-1-*naphthoic acid*, m. p. 204—205° (Found: C, 78·0; H, 6·0. $C_{13}H_{12}O_2$ requires C, 78·0; H, 6·0%).

Action of Phenylmagnesium Iodide on 3 : 7-*Dimethylnaphthalene*-1 : 2-*dicarboxylic Anhydride*.—Ethereal phenylmagnesium iodide [from iodobenzene (9·8 g.) and magnesium (1·2 g.)] was added portionwise to a benzene solution (300 ml.) of 3 : 7-dimethylnaphthalene-1 : 2-dicarboxylic anhydride (10 g.). The mixture was refluxed for 1 hr., left overnight at room temperature, then worked up as usual. The acid product was fractionally crystallised from benzene, to give 1-*benzoyl*-3 : 7-*dimethyl*-2-*naphthoic acid* (IV; R = H) in rods (5 g.), m. p. 231—232° (Found: C, 78·7; H, 5·0. $C_{20}H_{16}O_3$ requires C, 78·9; H, 5·3%). The *ethyl ester*, obtained by ethanol and hydrogen chloride and crystallised from ethanol, had m. p. 146—147° (Found: C, 79·7; H, 6·0. $C_{22}H_{20}O_3$ requires C, 79·5; H, 6·1%).

The benzene mother-liquor was concentrated, and the precipitated mixture of acids (m. p. 192—194°) was repeatedly crystallised from methanol, to give 2-*benzoyl*-3 : 7-*dimethyl*-1-*naphthoic acid* (V; R = H) in needles, m. p. 217—218° (1·8 g.), depressed to 190—200° on admixture with its isomer (Found: C, 79·3; H, 5·5%).

1-*Benzoyl*-3 : 7-*dimethylnaphthalene*.—(i) 3 : 7-Dimethyl-1-naphthoyl chloride (prepared by thionyl chloride) was distilled in a vacuum (180—185°/5 mm.), and the product crystallised from light petroleum (b. p. below 40°); the *chloride* had m. p. 57—58° (Found: Cl, 16·8. $C_{13}H_{11}OCl$ requires Cl, 16·2%). It (2 g.) was dissolved in benzene (4 g.) and carbon disulphide (12 ml.), treated portionwise with aluminium chloride (2 g., 1·5 mol.), then refluxed for 8 hr. The mixture was worked up as usual, and the product distilled (b. p. 230—235°/2 mm.). On crystallisation from light petroleum (b. p. below 40°) 1-*benzoyl*-3 : 7-*dimethylnaphthalene* was obtained in needles (19%), m. p. 84—85° (Found: C, 87·8; H, 6·1. $C_{19}H_{16}O$ requires C, 87·7; H, 6·2%).

(ii) 1-Benzoyl-3 : 7-dimethyl-2-naphthoic acid (1 g.) was decarboxylated with copper-bronze (0·2 g.) in quinoline (2 ml.) (nitrobenzene-bath) in the usual manner. The product was

[10] Weissgerber and Kruber, *Ber.*, 1919, **52**, 346.

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extracted with alcohol, then crystallised from light petroleum (b. p. below 40°) to give 1-benzoyl-3 : 7-dimethylnaphthalene, m. p. and mixed m. p. 84—85° (82%).

Its 2 : 4-*dinitrophenylhydrazone* crystallised from pyridine to give the α-*isomer* in dark red aggregates, m. p. 244—246° (Found: N, 13·2. $C_{25}H_{20}O_4N_4$ requires N, 12·7%). The pyridine mother-liquor precipitated, on dilution with water, the β-*isomer*, which crystallised from ethanol in orange rods, m. p. 231—232°, depressed to 210—225° on admixture with the α-isomer (Found: N, 11·9%).

2-*Benzoyl*-3 : 7-*dimethylnaphthalene*.—This *ketone* was obtained in 82% yield by decarboxylation of 2-benzoyl-3 : 7-dimethyl-1-naphthoic acid as above. It crystallised from light petroleum (b. p. 60—70°) in needles, m. p. 125—126° (Found: C, 87·6; H, 6·2%). Its 2 : 4-dinitrophenylhydrazone gave the α-*isomer* in red needles (from acetic acid), m. p. 235—236° (Found: N, 12·7%), and the β-*isomer* in yellow needles (from ethanol), m. p. 207—209°, depressed to 180—190° on admixture with the α-isomer (Found: N, 13·6%).

1-(α-*Hydroxy*-αα-*diphenylmethyl*)-3 : 7-*dimethylnaphthalene*.—Phenylmagnesium bromide [from bromobenzene (0·72 g.) and magnesium (0·11 g.)] was refluxed with 1-benzoyl-3 : 7-dimethylnaphthalene (1 g.) in benzene (20 ml.) for 2 hr., left at room temperature overnight, then worked up as usual. 1-(α-*Hydroxy*-αα-*diphenylmethyl*)-3 : 7-*dimethylnaphthalene* (63% yield) had m. p. 173—174° (from methanol) (Found: C, 88·4; H, 6·3; active H, 0·23. $C_{25}H_{22}O$ requires C, 88·7; H, 6·55; active H, 0·29%).

Alkali Fission of 1-*Benzoyl*-3 : 7-*dimethyl*-2-*naphthoic Acid*.—The acid (1 g.) was stirred with fused potassium hydroxide (1·5 g.) heated at 220—225° for 35 min., then worked up as usual. The acid product was boiled with water, filtered off while hot, and crystallised from benzene, to give 3 : 7-dimethyl-2-naphthoic acid (0·62 g.), m. p. 228°, depressed to 175—185° on admixture with 3 : 7-dimethyl-1-naphthoic acid (Found: C, 78·5; H, 6·2. Calc. for $C_{13}H_{12}O_2$: C, 78·0; H, 6·0%). Its anilide melted at 238°.[4] The aqueous mother-liquor was made alkaline, concentrated, and acidified to give benzoic acid (0·15 g.), identified by m. p. and mixed m. p.

Alkali Fission of 2-*Benzoyl*-3 : 7-*dimethyl*-1-*naphthoic Acid*.—The acid (0·6 g.) was heated with alkali (1 g.) at 235—250° for 15 min. The mixture was worked up as in the preceding experiment, to give benzoic (0·08 g.) and 3 : 7-dimethyl-1-naphthoic acid (0·34 g.), m. p. and mixed m. p. 204—205°.

Alkali Fission of 1- *and* 2-*Benzoyl*-3 : 7-*dimethylnaphthalene*.—(i) The former ketone (1·2 g.) was fused with potassium hydroxide (2 g.) at 240—250° for 20 min., then worked up as usual. The neutral product, m. p. 110—111° (from ethanol), proved to be 3 : 7-dimethylnaphthalene (0·6 g.) (Found: C, 92·1; H, 7·5. Calc. for $C_{12}H_{12}$: C, 92·3; H, 7·7%). Its picrate was obtained in yellow needles (from alcohol), m. p. 142—143°.[10] The concentrated alkaline filtrate was acidified to give a mixture from which 3 : 7-dimethyl-1-naphthoic, m. p. 204—205° (0·04 g.), and benzoic acid (0·12 g.) were isolated.

(ii) The latter ketone (1·2 g.) was similarly treated at 255—260°, to give 3 : 7-dimethylnaphthalene (0·48 g.), 3 : 7-dimethyl-2-naphthoic acid (0·12 g.), and benzoic acid (0·08 g.).

Di-(1-*benzoyl*-3 : 7-*dimethyl*-2-*naphthoic*) *Anhydride*.—A solution of the acid (0·6 g.) in dry carbon tetrachloride (30 ml.) was refluxed with phosphoric oxide (2 g.) for 4 hr. The mixture was decomposed with dilute hydrochloric acid, and the product crystallised from benzene, to give the *anhydride* (85%), m. p. 290—291° (Found: C, 81·2; H, 5·3. $C_{40}H_{30}O_5$ requires C, 81·3; H, 5·1%).

Di-(2-*benzoyl*-3 : 7-*dimethyl*-1-*naphthoic*) *anhydride* was similarly prepared (82%) (refluxing for 1 hr.; then storage overnight) and had m. p. 304—305° (from benzene) (Found: C, 80·9; H, 5·0%).

The anhydrides were converted into the acids when refluxed with 10% sodium hydroxide solution for 1 hr.

1-α-*Hydroxybenzyl*-3 : 7-*dimethylnaphthalene*-2-*carboxylic Lactone* (XII; R = H).—1-Benzoyl-3 : 7-dimethyl-2-naphthoic acid (2 g.), reduced by Martin's method (30 hr.), gave 1-α-*hydroxybenzyl*-3 : 7-*dimethylnaphthalene*-2-*carboxylic lactone* (64%) (from methanol), m. p. 196—197° (Found: C, 83·1; H, 5·6. $C_{20}H_{16}O_2$ requires C, 83·3; H, 5·6%).

2-α-*Hydroxybenzyl*-3 : 7-*dimethylnaphthalene*-1-*carboxylic Lactone* (XIII; R = H).—This *lactone* was similarly prepared (70%) by the reduction of 2-benzoyl-3 : 7-dimethyl-1-naphthoic acid. It had m. p. 213—214° (from methanol) (Found: C, 83·5; H, 5·5%).

The same lactones were obtained when the reduction was carried out with zinc dust and 10% sodium hydroxide solution in presence, or in absence, of toluene (20 hours' refluxing).

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Alkali Fission of 1- *and* 2-α-*Hydroxybenzyl*-3 : 7-*dimethylnaphthalene*-2- *and* -1-*carboxylic Lactone*.—The lactones were fused with potassium hydroxide at 240—250° for 10 and 20 min., respectively, then worked up as mentioned before. The product contained 3 : 7-dimethyl-2-naphthoic (71%) and 3 : 7-dimethyl-1-naphthoic acid (59%), respectively, together with a small amount of benzoic acid.

1-α-*Hydroxybenzyl*-3 : 7-*dimethyl*-2-*naphthylmethanol*.—1-Benzoyl-3 : 7-dimethyl-2-naphthoic acid (1 g.) was reduced with lithium aluminium hydride (1·5 g.) in ether (30 ml.) and benzene (40 ml.) (6 hours' refluxing), to give 1-α-*hydroxybenzyl*-3 : 7-*dimethyl*-2-*naphthylmethanol* (73%), m. p. 112—113° [from light petroleum (b. p. 60—70°)] (Found: C, 81·7; H, 7·1; active H, 0·59. $C_{20}H_{20}O_2$ requires C, 82·15; H, 6·9; active H, 0·68%).

2-α-*Hydroxybenzyl*-3 : 7-*dimethyl*-1-*naphthylmethanol* was similarly prepared (63%) from 2-benzoyl-3 : 7-dimethyl-1-naphthoic acid (0·5 g.) (10 hours' refluxing), and had m. p. 145—146° [from benzene–light petroleum (b. p. 40—60°)] (Found: C, 82·1; H, 6·6; active H, 0·72%).

When these alcohols (0·6 g.) were oxidised with potassium permanganate (0·5 g.) in 80% (v/v) aqueous acetone (100 ml.) overnight, they gave 1-benzoyl-3 : 7-dimethyl-2-naphthoic and 2-benzoyl-3 : 7-dimethyl-1-naphthoic acid, respectively.

1-*Benzyl*-3 : 7-*dimethyl*-2-*naphthoic Acid* (VI; R = H).—A mixture of 1-benzoyl-3 : 7-dimethyl-2-naphthoic acid (0·5 g.), anhydrous ethylene glycol (5 g.), sodium glycollate (from 0·5 g. of sodium), and 90% hydrazine hydrate (2 g.) was refluxed for 1·5 hr. at 115—120°. The condenser was removed and the temperature of the mixture raised to 220—230° and kept thereat for 6 hr. The whole was worked up as usual. The acid product was crystallised from benzene–light petroleum (b. p. 60—80°), to give 1-*benzyl*-3 : 7-*dimethyl*-2-*naphthoic acid* (30%), m. p. 190—191° (Found: C, 82·5; H, 6·2. $C_{20}H_{18}O_2$ requires C, 82·7; H, 6·25%). The neutral product crystallised from acetic acid, to give 1 : 2-*dihydro*-8 : 2′-*dimethyl*-1-*oxo*-4-*phenyl*-5 : 6-*benzophthalazine* (cf. VIII) (20%), m. p. 302—303° (Found: C, 79·4; H, 5·4; N, 9·2. $C_{20}H_{16}ON_2$ requires C, 80·0; H, 5·4; N, 9·3%). It contained no active hydrogen. Lowering the temperature of the reaction to 200° increased the amount of the neutral product.

2-*Benzyl*-3 : 7-*dimethyl*-1-*naphthoic Acid* (VII; R = H).—This was prepared by reducing 2-benzoyl-3 : 7-dimethyl-1-naphthoic acid with hydrazine hydrate (heating at 130° for 2 hr., then at 260—265° for further 2 hr.). The acid product was crystallised from benzene–light petroleum (b. p. 60—80°) to give 2-*benzyl*-3 : 7-*dimethyl*-1-*naphthoic acid* (34%), m. p. 203—204° (Found: C, 82·6; H, 6·4%). The neutral product crystallised from dioxan, to give 1 : 2-*dihydro*-5 : 3′-*dimethyl*-1-*oxo*-4-*phenyl*-6 : 8-*benzophthalazine* (cf. IX) (25%), m. p. 338—340° (Found: C, 79·3; H, 5·6; N, 9·3%).

2′ : 4-*Dimethyl*-1 : 2-*benzanthraquinone* (X or XI; R = H).—1(or 2)-Benzyl-2(or 1)-naphthoic acid (0·5 g.) was dissolved in concentrated sulphuric acid (8 ml.) and kept at room temperature for 2 hr., then worked up as usual. The benzanthrone formed, which failed to crystallise, was directly oxidised by sodium dichromate (0·7 g.) in acetic acid solution (20 ml.) (½ hr. at room temperature). The product precipitated on dilution with water crystallised from light petroleum (b. p. 40—60°), to give 2′ : 4-dimethyl-1 : 2-benzanthraquinone [11] in yellow needles (70%), m. p. 173° (Found: C, 83·2; H, 4·6. Calc. for $C_{20}H_{14}O_2$: C, 83·9; H, 4·9%).

Action of p-*Methoxyphenylmagnesium Bromide on* 3 : 7-*Dimethylnaphthalene*-1 : 2-*dicarboxylic Anhydride*.—The Grignard reagent [from *p*-bromoanisole (7 g.) and magnesium (0·8 g.)] was added to a solution of 3 : 7-dimethylnaphthalene-1 : 2-dicarboxylic anhydride (8 g.) in benzene (200 ml.)–ether (100 ml.), then refluxed for 1·5 hr. and worked up as usual. The acid product was refluxed with benzene, then extracted with sodium carbonate solution. The benzene solution gave on evaporation unchanged anhydride (0·2 g.). The acid precipitated on acidification of the alkaline extract was crystallised from the least amount of benzene, to give 1-p-*methoxybenzoyl*-3 : 7-*dimethyl*-2-*naphthoic acid* (31%), m. p. 202—203° (Found: C, 75·7; H, 5·7; OMe, 8·9. $C_{21}H_{18}O_4$ requires C, 75·4; H, 5·4; OMe, 9·3%). The benzene mother-liquor was evaporated, and the residue was triturated with hot light petroleum (b. p. 60—80°), then crystallised from benzene–light petroleum (b. p. 60—80°)to give 2-p-*methoxybenzoyl*-3 : 7-*dimethyl*-1-*naphthoic acid* (12%), m. p. 178—179°, depressed to 160—170° on admixture with the above isomer (Found: C, 75·5; H, 5·5; OMe, 8·6%).

Alkali Fission of 1-p-*Methoxybenzoyl*-3 : 7-*dimethyl*-2-*naphthoic Acid*.—The acid (0·5 g.) was stirred with fused potassium hydroxide (1 g.) at 230—240° for ½ hr., then worked up as usual. The product contained 3 : 7-dimethyl-2-naphthoic acid (0·2 g., 66%), and *p*-hydroxybenzoic

[11] Fieser and Fieser, *J. Amer. Chem. Soc.*, 1933, **55**, 3342.

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acid (0·08 g., 39%), m. p. 200—203°, raised to 204—206° on admixture with an authentic specimen.

Alkali Fission of 2-p-*Methoxybenzoyl*-3 : 7-*dimethyl*-1-*naphthoic Acid*.—The fusion was carried out as above, the product was crystallised from benzene to give 2-p-*hydroxybenzoyl*-3 : 7-*dimethyl*-1-*naphthoic acid*, m. p. 210—212° (62%), depressed to 180—190° on admixture with 3 : 7-dimethyl-1-naphthoic acid (Found: C, 75·1; H, 5·2; OMe, 0. $C_{20}H_{16}O_4$ requires C, 75·0; H, 5·0%).

1-p-*Methoxybenzyl*-3 : 7-*dimethyl*-2-*naphthoic Acid* (VI; R = OMe).—A solution of 1-*p*-methoxybenzoyl-3 : 7-dimethyl-2-naphthoic acid (1 g.) in 10% sodium hydroxide solution (50 ml.) was refluxed with zinc dust (2 g.) for 20 hr., then worked up as usual, to give 1-p-*methoxybenzyl*-3 : 7-*dimethyl*-2-*naphthoic acid* in needles, m. p. 225—226° (from benzene) (0·35 g., 36%) (Found: 78·7; H, 6·5; OMe, 9·6. $C_{21}H_{20}O_3$ requires C, 78·7; H, 6·3; OMe, 9·7%). The neutral product crystallised from methanol, to give 1-α-*hydroxy*-p-*methoxybenzyl*-3 : 7-*dimethylnaphthalene*-2-*carboxylic lactone* in needles, m. p. 202—203° (0·2 g., 20%) (Found: C, 78·7; H, 5·9; OMe, 9·3. $C_{21}H_{18}O_3$ requires C, 79·2; H, 5·7; OMe, 9·7%).

2-p-*Methoxybenzyl*-3 : 7-*dimethyl*-1-*naphthoic Acid* (VII; R = OMe).—The corresponding keto-acid (0·6 g.) was similarly reduced with zinc dust (2 g.) to give 2-p-*methoxybenzyl*-3 : 7-*dimethyl*-1-*naphthoic acid*, m. p. 212—213° [from benzene–light petroleum (b. p. 40—60°)] (0·2 g.; 34%) (Found: C, 78·8; H, 6·3; OMe, 9·0%).

6-*Methoxy*-2′ : 4-*dimethyl*-1 : 2-*benzanthraquinone* (X; R = OMe).—A solution of 1-*p*-methoxybenzyl-3 : 7-dimethyl-2-naphthoic acid (0·5 g.) in concentrated sulphuric acid (6 ml.) was left at room temperature (30—32°) for 4 hr., then worked up as usual. The resulting benzanthrone was oxidised with sodium dichromate (0·7 g.) in acetic acid (15 ml.) as mentioned above. On crystallisation from ethanol 6-*methoxy*-2′ : 4-*dimethyl*-1 : 2-*benzanthraquinone* was obtained in brownish-yellow needles, m. p. 165—166° (0·35 g., 70%) (Found: C, 79·5; H, 4·9; OMe, 9·6. $C_{21}H_{16}O_3$ requires C, 79·7; H, 5·1; OMe, 9·8%). It gave a blue solution with concentrated sulphuric acid.

7-*Methoxy*-2′ : 4-*dimethyl*-1 : 2-*benzanthraquinone* (XI; R = OMe).—2-*p*-Methoxybenzyl-3 : 7-dimethyl-1-naphthoic acid (0·2 g.) was similarly cyclised with concentrated sulphuric acid (4 ml.), then oxidised with sodium dichromate (0·3 g.) in acetic acid (10 ml.) at the b. p. for 5 min. The product crystallised from ethanol, to give 7-*methoxy*-2′ : 4-*dimethyl*-1 : 2-*benzanthraquinone* in fine yellow needles (0·15 g., 76%), m. p. 182—183°, depressed to 150—155° on admixture with the above isomer (Found: C, 79·0; H, 5·2; OMe, 9·3%). It gave a violet solution with concentrated sulphuric acid.

1-*Benzoyl*-3 : 7-*dimethyl*-2-*naphthoyl Chloride*.—The acid (1 g.) was treated with thionyl chloride (2 g.) for 1 hr.; the product crystallised from light petroleum (b. p. below 40°) to give 1-*benzoyl*-3 : 7-*dimethyl*-1-*naphthoyl chloride*, m. p. 163—165° (0·8 g., 76%) (Found: Cl, 11·0. $C_{20}H_{15}O_2Cl$ requires Cl, 11·0%).

2-*Benzoyl*-3 : 7-*dimethyl*-1-*naphthoyl chloride*, similarly prepared in 94% yield, had m. p. 149—150° [from light petroleum (b. p. 40—60°)] (Found: Cl, 10·75%).

1-(α-*Hydroxy*-αα-*diphenylmethyl*)-3 : 7-*dimethylnaphthalene*-2-*carboxylic Lactone* (XII; R = Ph).—(i) A solution of 1-benzoyl-3 : 7-dimethyl-2-naphthoyl chloride (1 g.) in a mixture of carbon disulphide (20 ml.) and benzene (1 g.) was treated with aluminium chloride (1 g.), refluxed for 4 hr., then worked up as usual. The neutral product was crystallised from ethanol, to give 1-(α-*hydroxy*-αα-*diphenylmethyl*)-3 : 7-*dimethylnaphthalene*-2-*carboxylic lactone* in needles, m. p. 225—226° (0·8 g., 71%) (Found: C, 85·3; H, 5·4. $C_{26}H_{20}O_2$ requires C, 85·7; H, 5·5%). It contained no active hydrogen. The m. p. was depressed to 200—212° on admixture with the original keto-acid.

(ii) Di-(1-benzoyl-3 : 7-dimethyl-2-naphthoic) anhydride (1 g.) was treated as in (i). The product contained a mixture of 1-benzoyl-3 : 7-dimethyl-2-naphthoic acid (0·35 g.) and 1-(α-hydroxy-αα-diphenylmethyl)-3 : 7-dimethylnaphthalene-2-carboxylic lactone (0·6 g.).

(iii) The Grignard reagent [from bromobenzene (1·25 g.) and magnesium (0·2 g.)] was added portionwise to a boiling solution of 1-benzoyl-3 : 7-dimethyl-2-naphthoic acid (1 g.) in benzene (50 ml.)–ether (10 ml.), refluxed for 4 hr., then worked up as usual. The neutral product was triturated with light petroleum (b. p. <40°), with few drops of methanol, then crystallised from ethanol to give 1-(α-hydroxy-αα-diphenylmethyl)-3 : 7-dimethylnaphthalene-2-carboxylic lactone (17% yield), m. p. 225—226° (decomp.), undepressed on admixture with the products obtained by methods (i) and (ii).

2-(α-*Hydroxy*-αα-*diphenylmethyl*)-3 : 7-*dimethylnaphthalene*-1-*carboxylic Lactone* (XIII; R = Ph).—This was prepared from 2-benzoyl-3 : 7-dimethyl-1-naphthoyl chloride, the anhydride, or the free acid by the three methods adopted for its isomer in 73, 72, and 34% yield, respectively. It crystallised from ethanol in needles, m. p. 231—232°, depressed to 190—200° when admixed with its isomer (Found: C, 85·1; H, 5·6%). It contained no active hydrogen.

Both lactones were recovered unchanged when refluxed with 10% alcoholic potassium hydroxide solution for 12 hr.

Alkali Fission of 1-(α-*Hydroxy*-αα-*diphenylmethyl*)-3 : 7-*dimethylnaphthalene*-2-*carboxylic Lactone*.—The lactone (0·4 g.) was stirred with fused potassium hydroxide (1 g.) at 265—270° for 20 min., then worked up as usual. The acid product crystallised from benzene to give 3 : 7-dimethyl-2-naphthoic acid in 90% yield. A small amount of crude benzoic acid was isolated.

Alkali Fission of 2-(α-*Hydroxy*-αα-*diphenylmethyl*)-3 : 7-*dimethylnaphthalene*-1-*carboxylic Lactone*.—When the fusion was carried out as above, 3 : 7-dimethyl-1-naphthoic acid was obtained in 73% yield, together with a small amount of crude benzoic acid.

A'in Shams University, Cairo, Egypt. [*Received, July 10th*, 1958.]

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204. β-*Aroylpropionic Acids. Part X.** *Conversion of* γ-*Aryl*-β-*phenylbutyrates into Polynuclear Compounds.*

By F. G. Baddar, Abdallah M. Fleifel, and Sayed Sherif.

Reduced β-benzoyl-β-phenyl- and β-phenyl-β-*p*-toluoyl-propionic acids are converted into 2 : 3-benzofluorenones. These are converted, by alkali fusion and recyclisation of the resulting acids, into the corresponding 1 : 2-benzofluorenones.

The crude ester (I; R = H), prepared by condensing ethyl βγ-diphenylbutyrate with ethyl oxalate in presence of potassium ethoxide,[1] was cyclised in 80% sulphuric acid to the 3 : 4-dihydro-anhydride (II; R = H). This was dehydrogenated with sulphur to the anhydride (III; R = H), then treated with anhydrous aluminium chloride to give 2 : 3-benzofluorenone-1-carboxylic acid (IV; R = H). This acid was decarboxylated with copper and quinoline to 2 : 3-benzofluorenone (V; R = H), which was reduced with lithium aluminium hydride to give 2 : 3-benzofluorenol (VI; R = H).

Attempts to convert 2 : 3-benzofluorenone-1-carboxylic acid into 1 : 2-benzofluorenone-3-carboxylic acid (VIII; R = H) by aluminium chloride–sodium chloride at 150° or 210° were unsuccessful. The conversion was, therefore, effected as follows:

The acid (IV; R = H) was fused with potassium hydroxide at 250° to give 3-*o*-carboxyphenyl-1-naphthoic acid (VII; R = H), which on cyclisation with concentrated sulphuric acid, gave 1 : 2-benzofluorenone-3-carboxylic acid (VIII; R = H). This was decarboxylated to 1 : 2-benzofluorenone (IX; R = H), then reduced with lithium aluminium hydride to 1 : 2-benzofluorenol (X; R = H).

When 2 : 3-benzofluorenone (V; R = H) was similarly fused with potassium hydroxide, it gave a 1 : 2-mixture of the acids (XI and XII; R = H). Cyclisation of these two acids with concentrated sulphuric acid gave 2 : 3- and 1 : 2-benzofluorenone, respectively.

When the crude ethoxalyl derivative (I; R = H) was refluxed with 20% (v/v) sulphuric acid,[1] it gave 3 : 4-dihydro-3-phenyl-1-naphthoic acid, which was dehydrogenated with sulphur to 3-phenyl-1-naphthoic acid, then decarboxylated to 2-phenylnaphthalene.

A similar series of reactions with the ethoxalyl ester (I; R = Me) gave 2′-methyl-2 : 3-benzofluorenone-1- (IV; R = Me) and 3′-methyl-1 : 2-benzofluorenone-3-carboxylic acid (V; R = Me) and 2-methyl-6-phenylnaphthalene.

Alkali fission of 2 : 3-benzofluorenone-1-carboxylic acid and 2 : 3-benzofluorenone to

* Part IX, preceding paper.

[1] Baddar and Warren, *J.*, 1939, 944.

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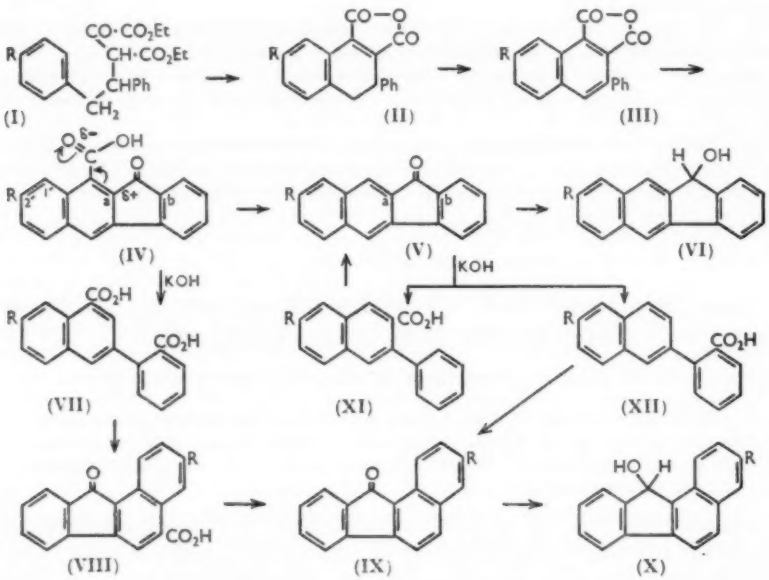
give 3-*o*-carboxyphenyl-1-naphthoic acid, and a mixture of *o*-β-naphthylbenzoic acid and 3-phenyl-2-naphthoic acid, respectively, indicates that the mode of fission is governed by the electron density on carbon atoms a and b.[2,3]

Cyclisation of the dicarboxylic acids (VII) to give only the 1 : 2-benzofluorenone-3-carboxylic acids (VIII) cannot be attributed to the steric effect of the bulky carboxyl



group, since even *o*-β-naphthylbenzoic acid (XII; R = H) gave only 1 : 2-benzofluorenone on cyclisation. It appears, therefore, that this is due to the fact that position 1 in the naphthalene nucleus is more susceptible to electrophilic attack than position 3.

Experimental

Ethyl βγ-diphenylbutyrate was obtained from βγ-diphenylbutyric acid [4] as an oil (87%), b. p. 190—195°/3 mm., $n_D^{21.5}$ 1·5460 (Found: C, 80·9; H, 7·45. $C_{18}H_{20}O_2$ requires C, 80·6; H, 7·5%).

3 : 4-*Dihydro*-3-*phenylnaphthalene*-1 : 2-*dicarboxylic Anhydride*.—Finely powdered potassium (1·9 g., 1 g.-equiv.) was covered with dry ether (100 ml.), allowed to react with absolute ethanol (3·5 ml.), then treated with freshly distilled ethyl oxalate (10·9 g., 1·5 mol.), followed by ethyl βγ-diphenylbutyrate (13·5 g., 1 mol.). The mixture was left overnight, then refluxed for 7 hr. and worked up as usual.[1] The crude ester (I) (20 g.) was heated on the water-bath with 80% (v/v) sulphuric acid (200 ml.) for 0·5 hr. The whole was poured on ice and the product filtered off (10·5 g.). Crystallisation from benzene–light petroleum (b. p. 40—60°) gave **3 : 4-*dihydro*-3-*phenylnaphthalene*-1 : 2-*dicarboxylic anhydride***, m. p. 144—145° (Found: C, 78·3; H, 4·5. $C_{18}H_{12}O_3$ requires C, 78·25; H, 4·4%). The ***dimethyl ester***, obtained in 70% yield by the action of diazomethane on the freshly precipitated acid, crystallised from benzene–light petroleum (b. p. 40—60°) in needles, m. p. 97—98° (Found: C, 75·0; H, 5·5; OMe, 19·1. $C_{20}H_{18}O_4$ requires C, 74·5; H, 5·6; 2OMe, 19·2%).

3-*Phenylnaphthalene*-1 : 2-*dicarboxylic Anhydride*.—The above dihydro-anhydride (1 g., 1 mol.) and sulphur (0·14 g., 1·2 g.-equiv.) were heated together at 205—210° for 10 hr. The product (0·8 g., 81%) crystallised from benzene to give **3-*phenylnaphthalene*-1 : 2-*dicarboxylic***

[2] Lea and Robinson, *J.*, 1926, 2351; Baddar and Gindy, *J.*, 1948, 1231.
[3] Olifson, *J. Gen. Chem.* (*U.S.S.R.*), 1939, **9**, 36; preceding paper.
[4] Ali, Desai, Hunter, and Mohammed, *J.*, 1937, 1013.

anhydride in yellow needles, m. p. 201—202° (Found: C, 79·05; H, 3·8. $C_{18}H_{10}O_3$ requires C, 78·8; H, 3·7%). The *dimethyl ester* had m. p. 84—85° (from methanol) (70%) (Found: C, 75·0; H, 5·05; OMe, 19·1. $C_{20}H_{16}O_4$ requires C, 75·0; H, 5·0; 2OMe, 19·4%).

2 : 3-*Benzofluorenone*-1-*carboxylic Acid*.—(i) A powdered mixture of the anhydride (2·2 g., 1 mol.) and aluminium chloride (5 g.) was added portionwise to cooled nitrobenzene (36 ml.) at <10°. The mixture was heated at 55—60° for 6 hr., then worked up as usual. The acid produced (1·7 g., 77%) was digested with hot benzene, then crystallised from xylene to give 2 : 3-*benzofluorenone*-1-*carboxylic acid* in orange-yellow needles, m. p. 244—245° (Found: C, 78·8; H, 3·5. $C_{18}H_{10}O_3$ requires C, 78·8; H, 3·7%). It gave a green colour with concentrated sulphuric acid. (ii) The same acid was obtained in 50% yield by heating the anhydride (0·5 g.) with aluminium chloride (5 g.) and sodium chloride (1 g.) at 150—155° for 90 min. 2 : 3-*Benzofluorenone*-1-*carboxylic acid* 2 : 4-*dinitrophenylhydrazone* crystallised from dioxan or acetic acid in orange-red crystals, m. p. 315—316° (Found: C, 63·4; H, 2·9; N, 11·7. $C_{24}H_{14}O_6N_4$ requires C, 63·4; H, 3·1; N, 12·3%). The *methyl ester* was obtained in yellow needles (86%) (from methanol), m. p. 152—153° (Found: C, 79·0; H, 4·2; OMe, 11·4. $C_{19}H_{12}O_3$ requires C, 79·15; H, 4·2; OMe, 10·8%).

2 : 3-*Benzofluorenone*.—2 : 3-Benzofluorenone-1-carboxylic acid was decarboxylated in 74% yield by copper-bronze and quinoline (1 hr.) in the usual manner. 2 : 3-Benzofluorenone had m. p. 152—153° (from ethanol), undepressed when admixed with an authentic specimen[5] (Found: C, 88·4; H, 4·35. Calc. for $C_{17}H_{10}O$: C, 88·7; H, 4·4%).

2 : 3-*Benzofluorenol*.—A solution of 2 : 3-benzofluorenone (0·5 g.) in dry thiophen-free benzene (20 ml.) was reduced with lithium aluminium hydride (0·4 g.) in dry ether (10 ml.) (5 hr. on water-bath), and worked up as usual.[6] The product (0·4 g., 79%), crystallised from benzene, gave 2 : 3-benzofluorenol, m. p. 185°, undepressed on admixture with an authentic specimen.[7]

Alkali Fission of 2 : 3-*Benzofluorenone*-1-*carboxylic Acid*.—The fluorenone (0·6 g., 1 mol.) was heated with fused potassium hydroxide (0·9 g.) at 240—250° for 1 hr. The acid product (0·4 g., 63%), crystallised from ethanol–benzene, gave 3-*o*-carboxyphenyl-1-naphthoic acid, m. p. 266—267° (Found: C, 73·6; H, 4·2. Calc. for $C_{18}H_{12}O_4$: C, 74·0; H, 4·1%). Baumgarten and Olshausen [8a] and Potts [8b] give m. p.s 267—268° and 261—262°, respectively.

Methyl 1 : 2-*Benzofluorenone*-3-*carboxylate*.—3-*o*-Carboxyphenyl-1-naphthoic acid (0·2 g.) was dissolved in concentrated sulphuric acid (2 ml.), left overnight, then worked up as usual. The acid was directly esterified to give the *methyl ester* (0·17 g., 86%) in orange needles [from benzene–light petroleum (b. p. 40—60°)], m. p. 163—164°, depressed to 135—140° when admixed with methyl 2 : 3-benzofluorenone-1-carboxylate (Found: C, 79·6; H, 4·3; OMe, 10·6. $C_{19}H_{12}O_3$ requires C, 79·15; H, 4·2; OMe, 10·8%).

1 : 2-*Benzofluorenone*.—1 : 2-Benzofluorenone-3-carboxylic acid was decarboxylated with copper-bronze and quinoline in the usual manner (74%). It crystallised from ethanol in orange needles, m. p. 132—133°, undepressed when admixed with an authentic specimen [9] (Found: C, 88·6; H, 4·45. Calc. for $C_{17}H_{10}O$: C, 88·7; H, 4·4%).

1 : 2-*Benzofluorenol*.—1 : 2-Benzofluorenone was reduced in 79% yield with lithium aluminium hydride in benzene–ether as previously mentioned for 2 : 3-benzofluorenol. It had m. p. 166—167° (from ethanol), not depressed when mixed with an authentic specimen.[10]

Alkali Fission of 2 : 3-*Benzofluorenone*.—The fluorenone (1 g.) was heated with potassium hydroxide (1·5 g.) at 205—210° for 1 hr. The product (0·9 g.), m. p. 140—155°, was fractionally crystallised from acetic acid, to give *o*-β-naphthylbenzoic acid (0·6 g.), m. p. 190°, undepressed on admixture with an authentic specimen.[11] Ring closure of this acid with concentrated sulphuric acid at room temperature gave 1 : 2-benzofluorenone.[9]

The acetic acid mother-liquor was diluted with water; the precipitated acid crystallised from ether–light petroleum (b. p. 40—60°) to give 3-*phenyl*-2-*naphthoic acid* (0·3 g.), m. p. 173—174°, depressed to 150—155° when admixed with its isomer (Found: C, 82·2; H, 5·0. $C_{17}H_{12}O_2$ requires C, 82·2; H, 4·9%). Cyclisation of this acid with concentrated sulphuric acid at room temperature afforded 2 : 3-benzofluorenone [5] (m. p. and mixed m. p.).

[5] Koelsch, *J. Amer. Chem. Soc.*, 1933, **55**, 3885.
[6] Baddar, Fahim, and Fleifel, *J.*, 1955, 2199.
[7] Thiele and Wanscheidt, *Annalen*, 1910, **376**, 269.
[8] (*a*) Baumgarten and Olshausen, *Ber.*, 1931, **64**, 925; (*b*) Potts, *J.*, 1956, 1269.
[9] Graebe, *Ber.*, 1896, **29**, 826.
[10] Bamberger and Kranzfeld, *Ber.*, 1885, **18**, 1934.
[11] Graebe, *Annalen*, 1904, **335**, 129.

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3 : 4-*Dihydro*-3-*phenyl*-1-*naphthoic Acid*.—This *acid* was obtained by refluxing the crude ester (I) (4 g.) with 20% (v/v) sulphuric acid (40 ml.) for 48 hr. It (2 g.) had m. p. 150—151° [from ether–light petroleum (b. p. 40—60°)] (Found: C, 81·3; H, 5·7. $C_{17}H_{14}O_2$ requires C, 81·6; H, 5·6%).

3-*Phenyl*-1-*naphthoic Acid*.—The above dihydro-acid (1 g.) and sulphur (0·15 g.) were heated at 205—210° for 5 hr., then worked up as usual. The acid product (0·8 g., 81%) crystallised from toluene to give **3-*phenyl*-1-*naphthoic acid***, m. p. 221—222° (Found: C, 81·7; H, 4·8. $C_{17}H_{12}O_2$ requires C, 82·2; H, 4·9%).

2-*Phenylnaphthalene*.—3-Phenyl-1-naphthoic acid was decarboxylated in 97% yield with copper-bronze and quinoline in the usual manner. 2-Phenylnaphthalene had m. p. 103—104° (from ethanol), not depressed when admixed with an authentic specimen.[12]

***Ethyl* β-*Phenyl*-γ-p-*tolylbutyrate*.**—This *ester* had b. p. 190—192°/25 mm. (85% yield), $n_D^{21\cdot5}$ 1·5410 (Found: C, 80·7; H, 7·9. $C_{19}H_{22}O_2$ requires C, 80·8; H, 7·85%).

3 : 4-*Dihydro*-7-*methyl*-3-*phenylnaphthalene*-1 : 2-*dicarboxylic Anhydride*.—Ethyl β-phenyl-γ-*p*-tolylbutyrate was converted into ethyl β-ethoxycarbonyl-α-oxo-γ-phenyl-δ-*p*-tolylvalerate in the usual manner. This was heated with 80% (v/v) sulphuric acid at 45—50° for 2 hr. The product (96%) crystallised from benzene–light petroleum (b. p. 50—70°) to give **3 : 4-*dihydro*-7-*methyl*-3-*phenylnaphthalene*-1 : 2-*dicarboxylic anhydride*** in pale yellow needles, m. p. 141—142° (Found: C, 78·1; H, 5·15. $C_{19}H_{14}O_3$ requires C, 78·6; H, 4·85%).

7-*Methyl*-3-*phenylnaphthalene*-1 : 2-*dicarboxylic Anhydride*.—Prepared by dehydrogenation of the above dihydro-anhydride with selenium at 205—210° for 8 hr., this *anhydride* (40%) crystallised from benzene in yellow needles, m. p. 241—242° (Found: C, 79·3; H, 4·3. $C_{19}H_{12}O_3$ requires C, 79·15; H, 4·2%).

2′-*Methyl*-2 : 3-*benzofluorenone*-1-*carboxylic Acid*.—Obtained in 86% yield by the action of aluminium chloride on 7-methyl-3-phenylnaphthalene-1 : 2-dicarboxylic anhydride as described above and crystallised from ethanol, **2′-*methyl*-2 : 3-*benzofluorenone*-1-*carboxylic acid*** formed orange needles, m. p. 253—254° (Found: C, 79·2; H, 4·3. $C_{19}H_{12}O_3$ requires C, 79·15; H, 4·2%).

2′-*Methyl*-2 : 3-*benzofluorenone*.—The preceding acid was decarboxylated in 70% yield with quinoline and copper-bronze. **2′-*Methyl*-2 : 3-*benzofluorenone*** was obtained in orange-yellow needles (from ethanol), m. p. 155—156° (Found: C, 88·5; H, 4·8. $C_{18}H_{12}O$ requires C, 88·5; H, 4·95%).

Alkali Fission of* 2′-*Methyl*-2 : 3-*benzofluorenone*-1-*carboxylic Acid*.**—The fluorenone was heated with fused potassium hydroxide at 205—210° for 10 min. **3-o-*Carboxyphenyl*-7-*methyl*-1-*naphthoic acid had m. p. 275—276° (from ethanol–benzene) (47% yield) (Found: C, 74·5; H, 4·5. $C_{19}H_{14}O_4$ requires C, 74·45; H, 4·6%).

3′-*Methyl*-1 : 2-*benzofluorenone*-3-*carboxylic Acid*.—3-*o*-Carboxyphenyl-7-methyl-1-naphthoic acid was cyclised with concentrated sulphuric acid. **3′-*Methyl*-1 : 2-*benzofluorenone*-3-*carboxylic acid*** crystallised from ethanol in orange crystals, m. p. 320—321°, depressed to 240—250° when admixed with 2′-methyl-2 : 3-benzofluorenone-1-carboxylic acid (Found: C, 79·0; H, 4·2%).

3′-*Methyl*-1 : 2-*benzofluorenone*.—This *ketone* was obtained (70%) by decarboxylation of the preceding acid and from ethanol formed orange-yellow crystals, m. p. 137—138° (Found: C, 88·5; H, 5·0%).

3 : 4-*Dihydro*-7-*methyl*-3-*phenyl*-1-*naphthoic Acid*.—The crude ethoxalyl derivative was refluxed with 20% (v/v) sulphuric acid as mentioned for the unsubstituted derivative. **3 : 4-*Dihydro*-7-*methyl*-3-*phenyl*-1-*naphthoic acid***, crystallised from benzene–light petroleum (b. p. 40—60°), had m. p. 234—235° (Found: C, 81·7; H, 6·0. $C_{18}H_{16}O_2$ requires C, 81·8; H, 6·1%).

7-*Methyl*-3-*phenyl*-1-*naphthoic Acid*.—This *acid* was obtained in 70% yield by dehydrogenating the dihydro-acid with selenium; it had m. p. 237—238° (from benzene), depressed to 220—225° on admixture with the dihydro-derivative (Found: C, 82·4; H, 5·4. $C_{18}H_{14}O_2$ requires C, 82·4; H, 5·4%).

2-*Methyl*-6-*phenylnaphthalene*.—The above acid was decarboxylated in 80% yield by the usual method. **2-*Methyl*-6-*phenylnaphthalene*** had m. p. 110—111° [from light petroleum (b. p. 50—70°)] (Found: C, 93·5; H, 6·5. $C_{17}H_{14}$ requires C, 93·5; H, 6·5%).

A'IN-SHAMS UNIVERSITY, CAIRO, EGYPT. [*Received, July 28th*, 1958.]

[12] Spring, *J.*, 1934, 1332.

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205. β-*Aroylpropionic Acids. Part XI.* The Action of Grignard Reagents on Phenylsuccinic Anhydride.*

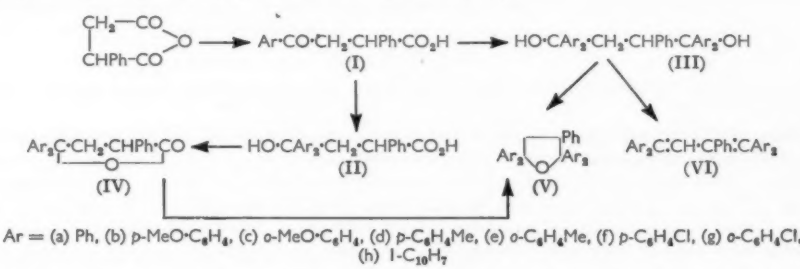
By Y. Akhnookh, W. I. Awad, and F. G. Baddar.

Arylmagnesium halides with phenylsuccinic anhydride give β-aroyl-α-phenylpropionic acid (I), γγ-diaryl-γ-hydroxy-α-phenylbutyric acid (II), isolated as its lactone (IV), and a neutral product from which a tetrahydrofuran (V) has been isolated. The same products are obtained when the anhydride is replaced by the β-aroyl-α-phenylpropionic acid corresponding to the Grignard reagent. However, arylmagnesium halides with β-aroyl-α-phenylpropionic esters or with diethyl phenylsuccinate give 3 : 3-diaryl-1-phenylprop-2-ene-1-carboxylic acids.

Propene-acids isomerise irreversibly to the lactones.

Previous work on methylsuccinic anhydride [1] has been extended to phenylsuccinic anhydride. Contrary to Weizmann *et al.*,[2] phenylmagnesium bromide with phenylsuccinic anhydride gave the lactone (IVa) and the furan (Va), but naphthylmagnesium bromide gave the keto-acid (Ih) and the lactone (IVh).

Similarly, when one or two mols. of *o*- or *p*-methoxyphenyl-, *o*- or *p*-tolyl-, or *o*- or *p*-chlorophenyl-magnesium bromide reacted with phenylsuccinic anhydride they gave the β-aroyl-α-phenylpropionic acid (I), the γγ-diaryl-γ-hydroxy-α-phenylbutyric acid (II) [isolated as its lactone (IV)], and a neutral product, from which a 2 : 2 : 5 : 5-tetra-aryltetrahydro-3-phenylfuran (V) was isolated (see Table 1).



Ar = (a) Ph, (b) *p*-MeO·C_6H_4, (c) *o*-MeO·C_6H_4, (d) *p*-C_6H_4Me, (e) *o*-C_6H_4Me, (f) *p*-C_6H_4Cl, (g) *o*-C_6H_4Cl, (h) 1-$C_{10}H_7$

However, although the neutral product isolated in the former case, gave analytical figures corresponding to 1 : 1 : 4 : 4-tetra-*p*-methoxyphenyl-2-phenylbuta-1 : 3-diene (VIb), its absorption spectrum ($\lambda_{max.}$ 291 mμ, ε 51,990) was different from that of 1 : 1 : 4 : 4-tetra-*p*-methoxyphenyl-buta-1 : 3-diene,[3] and this threw some doubt on its structure which needs further investigation.

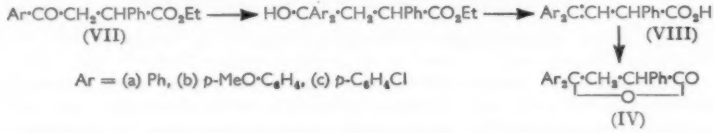
The structure of the β-aroyl-α-phenylpropionic acids was confirmed by the fact that they gave pyrylium salts,[4] and the β-benzoyl-, β-*p*-toluoyl-, and β-*p*-methoxybenzoyl-acids were identical with authentic specimens. The structure of the lactones and furans was established by identity with the products obtained when phenylsuccinic anhydride was replaced by β-aroyl-α-phenylpropionic acids (I). The lactones (IVa, d, and f) with arylmagnesium halides gave the 2 : 2 : 5 : 5-tetra-aryltetrahydro-3-phenylfurans (Va, d, and f, respectively).

When β-aroyl-α-phenylpropionic esters (VIIa, b, and c) were used instead of the

* Part X, *J.*, preceding paper.

[1] Baddar, El-Assal, and Habashi, *J.*, 1957, 1690.
[2] Weizmann, Blum-Bergmann, and Bergmann, *J.*, 1935, 1370.
[3] Baddar and Sawires, *J.*, 1955, 4469.
[4] Wali, Khalil, Bhatia, and Ahmad, *Proc. Indian Acad. Sci.*, 1941, **14**, *A*, 139; Desai and Wali, *ibid.*, 1937, **6**, *A*, 135.

corresponding acids, 3 : 3-diaryl-1-phenylprop-2-ene-1-carboxylic acids (VIIIa, b, and c, respectively) were obtained according to the following scheme:



The same propene-acids were obtained when the β-aroyl-α-phenylpropionic esters were replaced by diethyl phenylsuccinate.

The structure of the lactones, furans, and propene-acids was further confirmed by the identity of their absorption spectra with those previously reported.[3,5]

Attempts to isomerise the lactones (IVa, b, and f) to the corresponding propene-acids (VIII) by boiling with hydrochloric–acetic acid [6] were not successful. However, when the propene-acids were treated in the same manner, they were converted into the lactones in almost quantitative yield.

TABLE 1.

Ar in ArMgX (1 mol.)	Yields * (%) of I	IV	V	VI	Ar in ArMgX (1 mol.)	Yields * (%) of I	IV	V
Ph	12	22	3·5	—	*o*-Me·C₆H₄	22	4·7	1·6 †
p-MeO·C₆H₄	21	6	—	1·4?	*p*-Cl·C₆H₄	40	13	0·7
o-MeO·C₆H₄	18	9	1·4	—	*o*-Cl·C₆H₄	15	6	3·5 †
p-Me·C₆H₄	47	6	1·2	—	1-C₁₀H₇	41	8	1·2 †

* Calc. on crude product. † The neutral portion was an oil. ? structure not rigidly established.

EXPERIMENTAL

The procedure described in the first experiment was adopted with slight modification in the others.

Action of Phenylmagnesium Bromide on Phenylsuccinic Anhydride.—An ethereal solution (40 ml.) of phenylmagnesium bromide [from bromobenzene (7·85 g., 1 mol.)] was added dropwise (20 min.) to a boiling solution of phenylsuccinic anhydride (8·8 g., 1 mol.) in dry, thiophen-free benzene (100 ml.). The mixture was refluxed for a further 3 hr., left overnight at room temperature, then treated with ammonium chloride solution. The ether–benzene layer was extracted with sodium hydroxide solution, and the alkaline solution (charcoal) was cooled and acidified. The precipitated acids were refluxed with benzene for 1·5—2 hr., solvent was removed, and the semi-solid residue was extracted with cold sodium carbonate solution. The insoluble viscous oil solidified on trituration with cold alcohol. On crystallisation from benzene–light petroleum (b. p. 40—60°) *αγγ*-triphenylbutyrolactone (IV*a*) was obtained (*ca.* 3·5 g.), m. p. 162°, undepressed on admixture with an authentic specimen prepared by the method of Weizman *et al.*[3]

The sodium carbonate solution gave on acidification an acid (*ca.* 1·6 g.), which on crystallisation from benzene–light petroleum (b. p. 40—60°) gave γ-oxo-αγ-diphenylbutyric acid (Ia), m. p. 153°, undepressed on admixture with a specimen prepared according to Hann and Lapworth.[7] The neutral product in the ether–benzene layer was refluxed for 1—2 hr. with 20% sodium hydroxide solution to remove any lactone, and the insoluble oil (*ca.* 0·8 g.) was re-extracted with benzene. It was refluxed with acetic acid for 1 hr., then allowed to crystallise, giving *tetrahydro*-2 : 2 : 3 : 5 : 5-*pentaphenylfuran* (Va), m. p. 180° (Found: C, 89·7; H, 6·4. $C_{34}H_{28}O$ requires C, 90·2; H, 6·2%). The experiment was repeated with other aryl-magnesium bromide, with results given in Table 2.

Action of Grignard Reagents on β-Aroyl-α-phenylpropionic Acids.—The above experiment was repeated with β-aroyl-α-phenylpropionic acids instead of phenylsuccinic anhydride in the usual manner; the results are in Table 3.

[5] Baddar, Habashi, and Sawires, *J.*, 1957, 1699.
[6] Baddar and El-Assal, *J.*, 1951, 431.
[7] Hann and Lapworth, *J.*, 1904, 1355.

XUM

When in this reaction phenylmagnesium bromide was treated with β-benzoyl-β-phenylpropionic acid even under more drastic conditions, the keto-acid was recovered unchanged.

Action of Grignard Reagents on γγ-Diaryl-α-phenylbutyrolactones.—The experiment was

TABLE 2.

Compd.	M. p.	Solv. for cryst.*	Formula	Found (%) C	Found (%) H	Found (%) Cl	Required (%) C	Required (%) H	Required (%) Cl
Ib	149° [a]	A	$C_{17}H_{16}O_4$	—	—	—	—	—	—
IVb	132	A	$C_{24}H_{22}O_4$	76·4	5·8	—	77·0	5·9	—
VIb?	262	B	$C_{30}H_{24}O_4$	82·6	6·1	—	82·3	6·2	—
Ic	152	A	$C_{17}H_{16}O_4$	71·6	5·7	—	71·8	5·7	—
IVc	172	A	$C_{24}H_{22}O_4$	76·9	5·9	—	77·0	5·9	—
Vc	208	B	$C_{30}H_{26}O_5$	78·9	6·3	—	78·7	6·3	—
Id	151 [b]	A	$C_{17}H_{16}O_3$	—	—	—	—	—	—
IVd	142	A	$C_{24}H_{22}O_3$	83·8	6·3	—	84·2	6·5	—
Vd	228	B	$C_{30}H_{26}O$	89·9	7·2	—	89·7	7·1	—
Ie	116	A	$C_{17}H_{16}O_3$	75·6	6·0	—	76·1	6·0	—
IVe	125	A	$C_{24}H_{22}O_3$	84·1	6·5	—	84·2	6·5	—
Ve	Oil	—	—	—	—	—	—	—	—
If	160	A	$C_{16}H_{13}O_3Cl$	67·1	4·4	12·1	66·5	4·5	12·3
IVf	181	A	$C_{23}H_{16}O_3Cl_2$	69·0	4·3	18·0	68·9	4·2	18·5
Vf	202	B	$C_{24}H_{24}OCl_4$	69·0	4·1	23·8	69·1	4·1	24·1
Ig	112	A	$C_{16}H_{13}O_3Cl$	66·3	4·4	12·6	66·5	4·5	12·3
IVg	172	A	$C_{23}H_{16}O_3Cl_2$	68·8	4·1	18·0	68·9	4·2	18·5
Vg	Oil	—	—	—	—	—	—	—	—
Ih	142	A	$C_{20}H_{16}O_3$	78·7	5·2	—	78·9	5·3	—
IVh	211	A	$C_{30}H_{22}O_2$	86·9	5·4	—	86·9	5·4	—
Vh	Oil	—	—	—	—	—	—	—	—

* A, Benzene–light petroleum (b. p. 40—60°). B, Acetic acid. ? Structure not rigidly established.
[a] Identical with an authentic specimen (Allen and Frame, *Canad. J. Res.*, 1932, **6**, 605. [b] Identical with an authentic specimen (Desai *et al.*[4]).

TABLE 3.

Ar in ArMgX	Reactants (g. = 1 mol.)	Keto-acid (g. = 1 mol.)	Products: Unchanged keto-acid (g.)	Lactone (g.)	Neutral (g.)
Ph	7·5	Ia 10·5	2·0	IVa 2·5	Va 1·1
p-MeO·C_6H_4 ...	9·3	Ib 12·4	1·2	IVb 3·1	VIb(?) 2·5
o-MeO·C_6H_4 ...	9·3	Ic 12·4	2·6	IVc 3·8	Vc 2·2
p-C_6H_4Me	9·7	Id 13·4	3·8	IVd 4·1	Vd 1·9
o-C_6H_4Me	9·7	Ie 13·4	3·2	IVe 3·6	Ve 2·1
p-C_6H_4Cl	9·5	If 12·7	2·4	IVf 3·7	Vf 2·8
o-C_6H_4Cl	9·5	Ig 12·7	2·8	IVg 2·9	Vg 3·1
1-$C_{10}H_7$	11·6	Ih 15·2	4·1	IVh 3·8	Vh 3·6

repeated in the usual manner with γγ-diaryl-α-phenylbutyrolactones (1 mol.) instead of phenylsuccinic anhydride. The alkaline extract gave no precipitate on acidification, indicating the absence of acid. Only the neutral product was obtained, as in Table 4.

TABLE 4.

Reactants: Ar in ArMgX, g.	Lactone (g. = 1 mol.)	Neutral product, g.
Ph ..... 22·5	IVa 13·0	Va 10·2
p-C_6H_4Me ..... 29·0	IVd 16·5	Vd 8·1
p-C_6H_4Cl ..... 28·6	IVf 17·0	Vf 7·8

Action of Grignard Reagents on Ethyl β-Aroyl-α-phenylpropionate.—(i) *Action of phenylmagnesium bromide on ethyl γ-oxo-αγ-diphenylbutyrate.* The Grignard reagent [from bromobenzene (7·8 g., 1 mol.)] was added to a benzene solution (60 ml.) of ethyl γ-oxo-αγ-diphenylbutyrate (14·1 g., 1 mol.), and the mixture worked up as usual. The *acid* (*ca.* 2·4 g.), precipitated from the sodium hydroxide extract, crystallised from benzene–light petroleum (b. p. 40—60°) to give 1 : 3 : 3-triphenylprop-2-ene-1-carboxylic acid (VIIIa), m. p. 166° (Found: C, 83·9; H, 5·9. $C_{22}H_{18}O_2$ requires C, 84·0; H, 5·8%). It discharged the colour of alkaline potassium permanganate.

The neutral fraction (*ca.* 1·6 g.) was boiled with sodium hydroxide solution, then refluxed with glacial acetic acid for 1 hr., and left to crystallise, giving tetrahydro-2 : 2 : 3 : 5 : 5-pentaphenylfuran (Va), m. p. and mixed m. p. 180°.

(ii) A similar experiment with *p*-methoxyphenylmagnesium bromide and ethyl γ-*p*-methoxyphenyl-γ-oxo-α-phenylbutyrate gave, as acid fraction (*ca.* 2·6 g.), 3 : 3-*di*-p-*methoxyphenyl*-1-*phenylprop*-2-*ene*-1-*carboxylic acid* (VIIIb), m. p. 141° [from benzene–light petroleum (b. p. 40—60°)] (Found: C, 77·3; H, 6·0. $C_{24}H_{22}O_4$ requires C, 77·0; H, 5·9%). It discharged the colour of alkaline potassium permanganate.

The neutral fraction (*ca.* 2·0 g.) gave the same product, m. p. and mixed m. p. 262°, as in the case of phenylsuccinic anhydride.

(iii) A similar experiment with *p*-chlorophenylmagnesium bromide and ethyl γ-*p*-chlorophenyl-γ-oxo-α-phenylbutyrate gave 3 : 3-*di*-p-*chlorophenyl*-1-*phenylprop*-2-*ene*-1-*carboxylic acid* (*ca.* 1·6 g.) (VIIIc), m. p. 200° [from benzene–light petroleum (b. p. 40—60°)] (Found: C, 68·8; H, 4·4; Cl, 18·3. $C_{22}H_{16}O_2Cl_2$ requires C, 68·9; H, 4·2; Cl, 18·5%) (discharged the colour of alkaline potassium permanganate), and tetrahydro-2 : 2 : 5 : 5-tetra-*p*-chlorophenyl-3-phenylfuran (Vf) (*ca.* 2·1 g.), m. p. and mixed m. p. 202°.

Action of Grignard Reagents on Diethyl Phenylsuccinate.—Similar experiments with 2 mols. of the Grignard reagent and diethyl phenylsuccinate (1 mol.) gave the same propene-acids (cf. Table 5).

TABLE 5.

Reactants			Products			
Ar in ArMgX, g. = 2 mols.		Et_2 phenylsuccinate (g.)	Propene acid, g.		Neutral, g.	
Ph	15·7	12·5	VIIIa	1·5	Va	2·5
p-MeO·C_6H_4	18·6	12·5	VIIIb	1·2	VIb	0·9?
p-C_6H_4Cl	19·0	12·5	VIIIc	0·8	Vf	1·0

Isomerisation of the Propene-acids to the Lactones.—When 1 : 3 : 3-triphenyl-, 3 : 3-di-*p*-methoxyphenyl-1-phenyl-, and 3 : 3-di-*p*-chlorophenyl-1-phenyl-prop-2-ene-1-carboxylic acid were dissolved in the least amount of boiling concentrated hydrochloric acid–acetic acid (1 : 1 v/v) and refluxed for 6 hr., they were converted almost quantitatively into the lactones, identified by their m. p.s and mixed m. p.s.

αγγ-Triphenyl-, γγ-di-*p*-methoxy-phenyl-α-phenyl-, and γγ-di-*p*-chlorophenyl-α-phenylbutyrolactone were unaffected when similarly treated.

A'IN SHAMS UNIVERSITY, CAIRO, EGYPT. [*Received, August 14th,* 1958.]

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206. 1-*Phenylnaphthalenes. Part V.* The Cyclisation of Diarylidenesuccinic Anhydrides to* 1-*Phenylnaphthalenes.*

By F. G. BADDAR, LANSON S. EL-ASSAL, N. A. DOSS, and in part (MRS.) AWATEF H. SHEHAB.

Dissimilarly substituted dibenzylidenesuccinic anhydrides are prepared by a two-step Stobbe condensation. They give, on cyclisation, a mixture of the corresponding two isomeric 1-phenylnaphthalenes in nearly equal proportions.

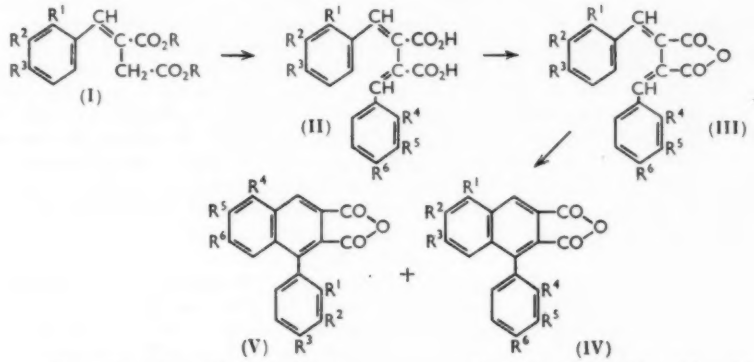
STOBBE condensation of *p*-chlorobenzaldehyde with diethyl succinate at −15° to −10° in presence of alcohol-free sodium ethoxide[1,2] gave di-*p*-chlorobenzylidenesuccinic acid (II*a*). Its anhydride (III*a*) cyclised in sunlight to 7-chloro-1-*p*-chlorophenylnaphthalene-2 : 3-dicarboxylic anhydride (IV*a*), identical with a specimen prepared by the self-condensation of *p*-chlorophenylpropiolic acid.[3]

* Part IV, 1958, 986.

[1] Baddar, El-Assal, and Gindy, Part I, *J.*, 1948, 1270.
[2] Baddar, El-Assal, and Doss, *J.*, 1955, 461.
[3] Baddar, El-Assal, and Doss, *J.*, 1959, 1027.

XUM

When *o*-methoxybenzaldehyde was condensed with dimethyl succinate in boiling alcoholic sodium ethoxide, it gave *o*-methoxybenzylidenesuccinic acid (I*b*; R = H). Its diethyl ester (I*b*; R = Et) was further condensed with *o*-chlorobenzaldehyde at low temperature in presence of sodium ethoxide [4] to give the diarylidenesuccinic acid (II*b*), whose anhydride (III*b*) cyclised in sunlight or when heated to give a mixture of 1-*o*-chlorophenyl-5-methoxy- (IV*b*) and 5-chloro-1-*o*-methoxyphenyl-naphthalene-2 : 3-dicarboxylic anhydride (V*b*) in nearly equal amounts. The structure of the anhydrides (IV*b* and V*b*) was established by their identity with specimens prepared by the action of *o*-chlorophenylpropioloyl chloride on *o*-methoxyphenylpropiolic acid.[3]



	R^1	R^2	R^3	R^4	R^5	R^6
a	H	H	Cl	H	H	Cl
b	MeO	H	H	Cl	H	H
c	H	H	MeO	H	H	H
d	H	$-O\cdot CH_2\cdot O-$		H	H	OMe

Similarly were prepared the acids (I*c*; R = H) and (II*c*) and the anhydride (III*c*), whose cyclisation afforded the naphthalene-anhydrides (IV*c*) and (V*c*) in nearly equal amount. The structures were proved as in other cases.

Piperonaldehyde gave an acid (I*d*: R = H) which had a much higher m. p. (200—201°) than that reported by Cornforth *et al.*[5] (m. p. 114—115°). The structure of this acid was established by its analysis and that of its dimethyl ester (I*d*; R = Me), and normal condensation of the ester to give the acid (II*d*). In addition, cyclisation of the anhydride (III*d*) in sunlight or by heat gave the anhydrides (IV*d*) and (V*d*) in nearly equal amounts. The dibasic acid derived from the former anhydride gave on decarboxylation 6 : 7-dimethoxy-1-*p*-methoxyphenylnaphthalene, identical with a specimen prepared by the decarboxylation of 1-*p*-methoxyphenyl-6 : 7-methylenedioxynaphthalene-3-carboxylic acid.[6] The identification of the anhydride (IV*d*) left no doubt concerning the structure of its isomer (V*d*).

Experimental

Di-p-chlorobenzylidenesuccinic Acid (II*a*).—A solution of *p*-chlorobenzaldehyde (12·5 g., 2 mol.) and diethyl succinate (8·6 g.; 1 mol.) in dry ether (30 ml.) was added to a suspension of finely powdered, alcohol-free sodium ethoxide (6·8 g., 2 mol.) in dry ether (50 ml.) at −15° to −10°. The temperature was kept thereat for 2 days and at 0° for further 2 days with occasional stirring. After the usual working up,[1,2] the product was digested with benzene, and the insoluble acid crystallised from acetic acid to give *di-p-chlorobenzylidenesuccinic acid* (*ca.* 3 g.), m. p. 225—226° (Found: C, 59·6; H, 3·5; Cl, 19·8. $C_{18}H_{12}O_4Cl_2$ requires C, 59·5; H, 3·3; Cl, 19·7%).

Di-p-chlorobenzylidenesuccinic Anhydride (III*a*).—The above acid (1 g.) was refluxed with

[4] Stobbe, *Annalen*, 1911, **380**, 50.
[5] Cornforth, Gordon, Hughes, and Lions, *J. Proc. Roy. Soc., N.S. Wales*, 1939, **72**, 238.
[6] El-Assal and Shehab, following paper.

acetyl chloride (6 ml.) for 2 hr. and then worked up as usual. The product (*ca.* 0·8 g.) was repeatedly crystallised from benzene–light petroleum (b. p. 40—60°), to give *di*-p-*chlorobenzylidenesuccinic anhydride* in lemon-yellow crystals, m. p. 203—204° (Found: C, 62·8; H, 2·9; Cl, 20·7. $C_{18}H_{10}O_3Cl_2$ requires C, 62·6; H, 2·9; Cl, 20·6%).

7-*Chloro*-1-p-*chlorophenylnaphthalene*-2 : 3-*dicarboxylic Anhydride* (IV*a*).—Di-*p*-chlorobenzylidenesuccinic anhydride (0·5 g.) was cyclised as usual with iodine in sunlight (10 days; October). The product crystallised from benzene, to give 7-*chloro*-1-p-*chlorophenylnaphthalene*-2 : 3-*dicarboxylic anhydride* in pale yellow needles, m. p. 266—267° (0·35 g.), undepressed on admixture with an authentic specimen prepared by the self-condensation of *p*-chlorophenylpropiolic acid [3] (Found: C, 62·7; H, 2·3; Cl, 20·5. $C_{18}H_8O_3Cl_2$ requires C, 63·0; H, 2·3; Cl, 20·7%).

Benzylidenesuccinic Acids (I; R = H).—The mixture of the aromatic aldehyde (27 g., 1 mol.), diethyl succinate (32 g., 1·1 mol.) and metallic sodium (5·5 g., 1·2 mol.) in absolute ethanol (150 ml.) was refluxed for 2·5 hr. Alcohol was then removed, 3% sodium hydroxide solution (350 ml.) was added, and the solution was then refluxed for 15 min. On cooling, the insoluble product was removed (either extracted with benzene or filtered off), and the cold alkaline solution (charcoal) was acidified. The precipitated acid was filtered off, washed with water, and dried. The dry acid product was then treated with boiling benzene and the insoluble product was filtered off, dried, and crystallised from a suitable solvent. The *products* are reported in Table 1. Acids (I*b* and *c*) were crystallised from 30% acetic acid, but (I*d*) from glacial acetic acid.

TABLE 1.

Acid	M. p.	Yield (%)	Formula	Found (%) C	Found (%) H	Required (%) C	Required (%) H
cis-I*b* †	210—211°	53	$C_{12}H_{12}O_5$	60·9	5·2	61·0	5·2
cis-I*c* †	202—203	57	$C_{12}H_{12}O_5$	61·3	5·35	,,	,,
I*d* [5]	200—201	96	$C_{12}H_{10}O_6$	57·9	3·95	57·6	4·0

† The *cis*-configuration was established by cyclisation to the corresponding 3-hydroxy-2-naphthoic acids (El-Abbady and El-Assal, *J.*, 1959, 1024).

Diethyl o-*Methoxybenzylidenesuccinate* (I*b*; R = Et).—The mixture of the acid (I*b*; R = H) (20 g.), absolute ethanol (70 ml.), benzene (30 ml.), and concentrated sulphuric acid (2 ml.) was refluxed for 15 hr., then worked up as usual. The product was distilled in a vacuum and the lemon-yellow viscous *diethyl* o-*methoxybenzylidenesuccinate* (*ca.* 18 g.), b. p. 280—285°/4 mm., was collected (Found: C, 65·5; H, 7·1. $C_{16}H_{20}O_5$ requires C, 65·75; H, 6·9%).

Diethyl p-*methoxybenzylidenesuccinate* (I*c*; R = Et), prepared as was its *o*-methoxy-isomer, had b. p. 285—290°/4 mm. (11 g.) (Found: C, 65·8; H, 7·0%).

Dimethyl Piperonylidenesuccinate (I*d*; R = Me).—A mixture of the acid (I*d*; R = H) (25 g.), dimethyl sulphate (50·5 g.), and potassium carbonate (100 g.) in acetone (150 ml.) was heated for 12 hr., then worked up as usual. The fraction of the product boiling at 224—228°/6 mm. was triturated with ether, giving a colourless solid. On crystallisation from benzene–light petroleum (b. p. 40—60°) it gave *dimethyl piperonylidenesuccinate* in rosettes (17 g.), m. p. 77—78° (Found: C, 60·25; H, 5·1. $C_{14}H_{14}O_6$ requires C, 60·4; H, 5·0%).

Dissimilarly Substituted Dibenzylidenesuccinic Acids (II).—A solution of the aromatic aldehyde (~ 7 g., 1 mol.) and the ester (I; R = Et) (1 mol.) in ether (*ca.* 25 ml.) was added to a suspension of sodium ethoxide (3·5 g., 1·1 mol.) in ether (*ca.* 130 ml.) at −18°, kept between −15° and −10° for 3 days, then finally at room-temperature (20—25°) for several hours with occasional stirring. The product was worked up as usual.[3] The product insoluble in benzene was crystallised from a suitable solvent and the results are summarised in Table 2.

TABLE 2.

Acid	Solvent	M. p.	Yield (%)	Found (%) C	Found (%) H	Found (%) Cl	Required (%) C	Required (%) H	Required (%) Cl
II*b*	Aq. AcOH	232—233°	52	63·15	4·1	9·8	63·6	4·2	9·9
II*c*	,,	231—232	87	69·8	5·0	—	70·4	4·9	—
II*d* *	AcOH	224—227	70	—	—	—	—	—	—

* The cooling in this case was at −18° to −15° for 24 hr. and then at 0° for a further 3 days. The acid was gradually transformed into its anhydride on repeated crystallisation from glacial acetic acid as indicated by the lowering of its m. p. and by a change of colour; it was best analysed as its anhydride.

α-o-*Chlorobenzylidene*-β-o-*methoxybenzylidenesuccinic Anhydride* (III*b*), prepared in the usual manner, had m. p. 98—100° [lemon-yellow crystals from benzene–light petroleum (b. p. below 40°)] (Found: C, 66·6; H, 3·85; Cl, 10·0. $C_{19}H_{13}O_4Cl$ requires C, 66·95; H, 3·8; Cl, 10·4%).

Cyclisation of α-o-*Chlorobenzylidene*-β-o-*methoxybenzylidenesuccinic Anhydride*.—(i) The anhydride (2 g.) was cyclised by iodine in sunlight in the usual manner (14 days, Ohio, U.S.A.). The product (*ca.* 1·5 g.) was fractionally crystallised, to give 1-o-*chlorophenyl*-5-*methoxynaphthalene*-2 : 3-*dicarboxylic anhydride* (IV*b*) in lemon-yellow crystals, m. p. 251—252°, undepressed on admixture with a specimen prepared by the action of *o*-chlorophenylpropioloyl chloride on *o*-methoxyphenylpropiolic acid [3] (Found: C, 67·3; H, 3·1; Cl, 10·7. $C_{19}H_{11}O_4Cl$ requires C, 67·35; H, 3·25; Cl, 10·5%). The benzene mother-liquor was concentrated and the precipitated product (*ca.* 0·55 g.) repeatedly crystallised from the same solvent, to give 5-*chloro*-1-o-*methoxyphenylnaphthalene*-2 : 3-*dicarboxylic anhydride* (V*b*), m. p. 199—200°, undepressed on admixture with a specimen prepared by the action of *o*-chlorophenylpropioloyl chloride on *o*-methoxyphenylpropiolic acid [3] (Found: C, 66·9; H, 3·25; Cl, 10·6%). (ii) The anhydride (III*b*) (2 g.) was heated at 280—290° for 2 hr., then worked up as in (i). The product (*ca.* 1·4 g.; m. p. 175—215°) precipitated from ether was fractionally crystallised from benzene to give 1-*o*-chlorophenyl-5-methoxy- (IV*b*) and 5-chloro-1-*o*-methoxy-phenylnaphthalene-2 : 3-carboxylic anhydride (V*b*), identified by m. p. and mixed m. p.

α-*Benzylidene*-β-p-*methoxybenzylidenesuccinic Anhydride* (III*c*).—This *compound* was obtained from the acid (5 g.) and acetyl chloride (15 ml.) in the usual manner as lemon-yellow crystals [from benzene–light petroleum (b. p. below 40°)], m. p. 153—154° (*ca.* 4·5 g.) (Found: C, 74·2; H, 4·8. $C_{19}H_{14}O_4$ requires C, 74·5; H, 4·6%).

Cyclisation of α-*Benzylidene*-β-p-*methoxybenzylidenesuccinic Anhydride*.—The above anhydride (III*c*) (2 g.) was cyclised with iodine in the usual manner (14 days; Ohio, U.S.A.). The product (*ca.* 1·8 g.), m. p. 210—220°, on fractional crystallisation from benzene, gave 1-p-*methoxyphenylnaphthalene*-2 : 3-*dicarboxylic anhydride* (V*c*) (*ca.* 0·5 g.) in lemon-yellow crystals, m. p. 259—260°, undepressed on admixture with a specimen prepared by the action of *p*-methoxyphenylpropioloyl chloride on phenylpropiolic acid [3] (Found: C, 74·8; H, 4·2. $C_{19}H_{12}O_4$ requires C, 75·0; H, 3·95%). Concentration of the original benzene mother-liquor precipitated a product (0·48 g.) which on repeated crystallisation from the same solvent gave 7-*methoxy*-1-*phenylnaphthalene*-2 : 3-*dicarboxylic anhydride* (IV*c*) in pale yellow crystals, m. p. 267—268°, undepressed on admixture with an authentic specimen [3] (Found: C, 74·85; H, 4·0%).

α-p-*Methoxybenzylidene*-β-*piperonylidenesuccinic Anhydride* (III*d*).—The *anhydride* (*ca.* 3·5 g.), prepared from its acid (II*d*) (4·5 g.) in the usual manner, was repeatedly crystallised from benzene in orange rosettes, m. p. 182—183° (Found: C, 68·6; H, 4·15; OMe, 8·4. $C_{20}H_{14}O_6$ requires C, 68·6; H, 4·0; OMe, 8·85%).

Cyclisation of α-p-*Methoxybenzylidene*-β-*piperonylidenesuccinic Anhydride*.—(i) The solution of the anhydride (III*d*) (1 g.) in benzene (10 ml.) was treated with iodine in the usual manner (14 days; Cairo). The precipitated product (*ca.* 0·2 g.), m. p. 272—274°, was boiled with 10% sodium hydroxide solution (5 ml.) to remove traces of the second isomer, and the insoluble product was filtered off, washed, and dried. On crystallisation from acetic acid, 7-*methoxy*-1-(3 : 4-*methylenedioxyphenyl*)*naphthalene*-2 : 3-*dicarboxylic anhydride* (V*d*) was obtained in light brown crystals, m. p. 277—278° (Found: C, 68·85; H, 3·75; OMe, 8·4. $C_{20}H_{12}O_6$ requires C, 68·9; H, 3·5; OMe, 8·9%). Distillation of the original benzene mother-liquor left a brown semi-solid, which on trituration with ether was transformed into crystals (*ca.* 0·3 g.), m. p. 272—274°. On repeated crystallisation from benzene it gave lemon-yellow 1-p-*methoxyphenyl*-6 : 7-*methylenedioxynaphthalene*-2 : 3-*dicarboxylic anhydride* (IV*d*) (0·25 g.), m. p. 275—276°, depressed on admixture with a specimen of its isomer (V*d*) (Found: C, 69·0; H, 3·6; OMe, 8·4%). (ii) The anhydride (III*d*) (1·5 g.) was heated at 205—210° (nitrobenzene-bath) for 3 hr. The glassy mass was triturated with ether, and the insoluble solid was filtered off (*ca.* 1·1 g.), then treated with boiling benzene. The insoluble product (*ca.* 0·5 g.) was treated as described in (i) and crystallised from acetic acid, to give 7-methoxy-1-(3 : 4-methylenedioxyphenyl)naphthalene-2 : 3-dicarboxylic anhydride identified by m. p. and mixed m. p. Concentration of the benzene solution precipitated a solid which after repeated crystallisation from the same solvent gave 1-*p*-methoxyphenyl-6 : 7-methylenedioxynaphthalene-2 : 3-dicarboxylic anhydride (0·52 g.), identified by m. p. and mixed m. p.

1-p-*Methoxyphenyl*-6 : 7-*methylenedioxynaphthalene*.—A solution of the above acid (0·2 g.) (prepared from its anhydride) in quinoline (5 ml.) was stirred with copper-bronze (0·1 g.) while

gradually heated to 205—210° (nitrobenzene-bath) during 30 min. The temperature was kept thereat for 30 min. during which a further amount of copper-bronze (0·1 g.) was added portionwise. The heating and stirring were continued for a further hour, then the whole was worked up as usual. The brown viscous oily product was transformed on trituration with light petroleum (b. p. 40—60°) into a solid, m. p. 103—104° (*ca.* 0·1 g.). On repeated crystallisation from the same solvent it gave 1-p-*methoxyphenyl*-6 : 7-*methylenedioxynaphthalene* in pale brown crystals, m. p. 108—109°, undepressed on admixture with a specimen prepared by the decarboxylation of 1-*p*-methoxyphenyl-6 : 7-methylenedioxynaphthalene-3-carboxylic acid [6] (Found: C, 77·8; H, 5·2; OMe, 13·6. $C_{18}H_{14}O_3$ requires C, 77·7; H, 5·0; OMe, 12·15%).

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CHEMISTRY DEPARTMENT, OHIO UNIVERSITY.
A'IN-SHAMS UNIVERSITY, CAIRO, EGYPT.

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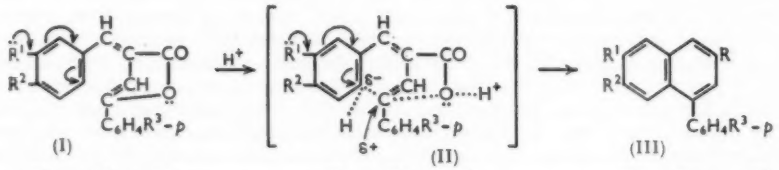
207. β-*Aroyl-α-arylmethylenepropionic Acids. Part I. Conversion of the Lactones of* β-*Aroyl-α-arylmethylenepropionic Acids into the Corresponding* 1-*Phenylnaphthalenes.*

By LANSON S. EL-ASSAL and (MRS.) AWATEF H. SHEHAB.

The lactones of β-aroyl-α-arylmethylenepropionic acids are converted into the corresponding 1-phenylnaphthalenes by three methods. However, some lactones fail to isomerise even under drastic conditions.

THE conversion of lactones (I) into 1-phenylnaphthalenes (III) was attempted by three methods, two of them described by Howell and Robertson [1] and by Haworth and Sheldrick [2] severally; the third was developed by the authors in this investigation. Those methods are: (i) Passing hydrogen chloride into a suspension of the lactone in boiling methanol for several hours. (ii) Leaving a chloroform solution of the lactone with iodine at room temperature for 5—15 days. (iii) Refluxing the lactone with a mixture of glacial acetic and concentrated hydrochloric acid for a period ranging from 20 minutes to 6 hours. In general, method (iii) proved superior as it gives purer products in shorter times (see Tables). Method (ii) is less often successful than method (i) and gave less pure products.



(I) (II) (III)

	R^1	R^2	R^3
a	$-O{\cdot}CH_2{\cdot}O-$		OMe
b	OMe	OMe	Cl
c	OMe	OMe	H
d	$-O{\cdot}CH_2{\cdot}O-$		Me
e	OMe	OMe	OMe
f	OMe	OMe	Me
g	H	OMe	OMe
h	H	OMe	H
i	H	H	OMe
j	H	H	H

The structure of methyl 4-*p*-methoxyphenyl-6 : 7-methylenedioxynaphthalene-2-carboxylate (III*a*; R = CO_2Me), obtained by method (i), followed because the derived acid (III*a*; R = CO_2H) was identical with that obtained by the isomerisation with method

[1] Howell and Robertson, *J.*, 1936, 587.
[2] Haworth and Sheldrick, *J.*, 1935, 636.

(iii), and decarboxylation of this acid gave 1-*p*-methoxyphenyl-6 : 7-methylenedioxynaphthalene (III*a*; R = H) identical with the decarboxylation product of 1-*p*-methoxyphenyl-6 : 7-methylenedioxynaphthalene-2 : 3-dicarboxylic acid which was obtained by the Stobbe condensation.[3]

Methyl 4-*p*-chlorophenyl-6 : 7-dimethoxynaphthalene-2-carboxylate (III*b*; R = CO_2Me) gave on hydrolysis its acid (III*b*; R = CO_2H), identical with the product obtained by method (iii). This acid was decarboxylated to 1-*p*-chlorophenyl-6 : 7-dimethoxynaphthalene (III*b*; R = H). When this compound was dechlorinated by palladised charcoal[4] in tetralin at 205—210°, it gave 6 : 7-dimethoxy-1-phenylnaphthalene[1] (III*c*; R = H).

By method (i) the lactones (I*d*, *e*, *f*) gave the esters (III; R = CO_2Me), which were hydrolysed to acids identical with those obtained by method (iii). These acids were decarboxylated to the naphthalenes (III; R = H) whose structures rest on analogy with the above two examples and those in the literature.[1,2]

Some lactones of type (I) failed to react by any of the three methods. When positions 3 and 4 in the benzylidene radical are occupied by electron-repelling substituents (3 : 4-methylenedioxy, 3 : 4-dimethoxy) the reaction is successful: but it failed with lactones (I*g*, *h*, *i*, *j*) even when attempted by pyrolysis, action of aluminium chloride in nitrobenzene at 20—25° or 100° for several hours or in a sodium chloride melt, or by iodine in chloroform at 20—25° or at the b. p.

The hydrogen chloride reaction appears to be initiated by the attack of a proton on the lactone-oxygen atom. Reaction then proceeds as indicated in formula (II), in a way similar to electrophilic substitution. Since the crude products of isomerisation by method (iii) were pure (m. p. only 1—2° low), the authors believe that the possibility of attachment at the carbon atom 2 is greatly diminished by steric factors.

Experimental

Preparation of the Lactones of β-*Aroyl*-α-*arylmethylenepropionic Acids.*—The mixture of the aromatic aldehyde (1 mol.) and dry sodium β-benzoylpropionate or its derivative (1 mol.) in acetic anhydride was heated on a boiling-water bath for several hours, left overnight, and then worked up as usual.[1,2] The *lactone* was then crystallised from a suitable solvent. The time of heating and the amount of acetic anhydride had a profound effect on the yield and the purity of the products (see Table 1).

Cyclisation of the Lactones (I).—*Method* (i). Dry hydrogen chloride was passed into a suspension of the lactone (I) in boiling methanol for several hours (complete discharge of the lactone colour). The solution was then concentrated and left to cool. The precipitated colourless ester was filtered off, washed with water, sodium carbonate solution, and water, and dried. Then the ester was crystallised from a suitable solvent. The results are in Table 2.

Method (ii). The solution of the lactone in chloroform was left in diffused light for several days at 20—25°, then washed with sodium thiosulphate solution and sodium carbonate solution. Acidification of the sodium carbonate solution precipitated the acid which was filtered off, washed, dried, and recrystallised. Table 3 gives the results. Lactones (I*a*, *b*, and *d*) gave only traces of acid (III). The crude product needed several crystallisations.

Method (iii). A suspension of lactone (I) in glacial acetic and concentrated hydrochloric acid was heated until the lactone colour disappeared. The precipitated colourless product was filtered off, washed with water, and digested in sodium carbonate solution. The alkaline solution was acidified and the precipitated acid filtered off, washed with water, dried, and recrystallised (Table 4). The products obtained by this method were identical with the hydrolysis products of the corresponding esters obtained by method (i) and with the acids obtained by method (ii).

1-p-*Methoxyphenyl*-6 : 7-*methylenedioxynaphthalene* (III*a*; R = H).—The solution of 1-*p*-methoxyphenyl-6 : 7-methylenedioxynaphthalene-3-carboxylic acid (III*a*; R = CO_2H) (0·25 g.)

[3] Baddar, El-Assal, Doss, and Shehab, 1016.
[4] Doss, unpublished work.

TABLE 1.

Lactone	Amounts: Salt (g.)	Ac_2O (ml.)	Time (hr.)	Solvent *	Colour	M. p.	Yield (%)
I*a*	5 [1, 6]	40	3	C_6H_6–Pet	Yellow	211—212°	65
I*b*	1·3 [7]	4	1	,,	Orange-yellow	182—183	63
I*c*	6 [8]	80	3	AcOH	Golden-yellow	131—132	81 [1]
I*d*	4·3 [9]	40	3	$CHCl_3$	Orange	214—215	98
I*e*	2·3 [1, 6]	20	6	AcOH	Orange-yellow	174—175	91
I*f*	2·15 [9]	30	3	,,	Orange	144—145	90
I*g*	2·3 [1, 6]	5	6	,,	Greenish-yellow	177—178	83
I*h*	2 [8]	5	3	C_6H_6	Orange-yellow	168—169	71 [5]
I*i*	2·3 [1, 6]	15	3	,,	Greenish-yellow	176—177	90 [1]
I*j*	6 [8]	15	6	AcOH	Orange-yellow	150—151	53 [5]

Lactone	Formula	Found (%): C	H	OMe	Cl	Required (%): C	H	OMe	Cl
I*a*	$C_{19}H_{14}O_5$	71·2	4·5	9·1	—	70·8	4·35	9·6	—
I*b*	$C_{19}H_{15}O_4Cl$	66·8	4·6	17·6	9·7	66·6	4·4	18·1	10·4
I*c*	$C_{19}H_{16}O_4$	—	—	—	—	—	—	—	—
I*d*	$C_{19}H_{14}O_4$	74·7	4·7	—	—	74·5	4·6	—	—
I*e*	$C_{20}H_{16}O_5$	71·3	5·5	27·0	—	71·0	5·3	27·5	—
I*f*	$C_{20}H_{16}O_4$	74·2	5·65	19·65	—	74·5	5·6	19·25	—
I*g*	$C_{19}H_{16}O_4$	74·3	5·3	19·6	—	74·0	5·2	20·1	—

* Pet = Light petroleum (b. p. 60—80°).

TABLE 2. *Method* (i), *giving esters* (III; R = CO_2Me).

Lactone No.	(g.)	Time (hr.)	MeOH (ml.)	M. p. [a]	Yield (%)	Formula	Found (%): C	H	OMe	Required (%): C	H	OMe
I*a*	1	2	15	154—155°	76	$C_{20}H_{16}O_5$	71·2	5·0	18·0	71·4	4·8	18·45
I*b*	0·5	6	30	165—166 [b]	80	$C_{20}H_{17}O_4Cl$ *	67·4	4·8	25·0	67·3	4·8	26·0
I*c*	—	4	—	124 [1]	—	—	—	—	—	—	—	—
I*d*	1	30	30	151—152 [c]	80	$C_{20}H_{16}O_4$	75·3	5·1	—	75·0	5·0	—
I*e*	0·5	8	30	139—140	96	$C_{21}H_{20}O_5$	71·65	5·75	35·1	71·5	5·7	35·2
I*f*	0·5	6	30	146—147	96	$C_{21}H_{20}O_4$	75·5	6·2	26·8	75·0	5·95	27·3

* Cl: Found, 10·2. Reqd., 9·7%. [a] Cryst. from MeOH, except as stated. [b] From C_6H_6. [c] From light petroleum (b. p. 60—70°).

TABLE 3. *Cyclisation by method* (ii).

Lactone No.	g.	I	$CHCl_3$ (ml.)	Time (days)	Solvent	M. p.	Yield (%)
I*c*	1·7	1·7	20	5	MeOH	265°	41·2 [1]
I*e*	0·5	0·2	10	5	AcOH	231—232	90
I*f*	1	0·4	20	15	,,	244—245	90

in quinoline (4 ml.) containing copper-bronze (0·1 g.) was refluxed for 30 min. More copper-bronze (0·1 g.) was added and heating continued for a further hour. Working up as usual and repeated crystallisation from light petroleum (b. p. 40—60°) gave 1-*p*-methoxyphenyl-6 : 7-methylenedioxynaphthalene (0·18 g.) in pale brown rosettes, m. p. 108—109°, undepressed on admixture with a specimen prepared by the decarboxylation of 1-*p*-methoxyphenyl-6 : 7-methylenedioxynaphthalene-2 : 3-dicarboxylic acid prepared by a two-step Stobbe condensation [3] (Found: C, 78·0; H, 5·2, OMe, 12·0. Calc. for $C_{19}H_{14}O_3$: C, 77·7; H, 5·0; OMe, 11·15%).

1-p-*Chlorophenyl*-6 : 7-*dimethoxynaphthalene* (III*b*; R = H).—The carboxylic acid (III*b*; R = CO_2H) (1 g.) and copper-bronze (2 × 0·4 g.) in quinoline (10 ml.) gave, after distillation, a fraction of b. p. 216—220°/4 mm. Crystallisation from light petroleum (b. p. <40°) gave 1-p-*chlorophenyl*-6 : 7-*dimethoxynaphthalene* (0·6 g.), m. p. 98—99° (Found: C, 72·3; H, 5·3; OMe, 20·1; Cl, 11·2. $C_{18}H_{15}O_2Cl$ requires C, 72·4; H, 5·4; OMe, 20·8; Cl, 11·9%).

[6] Borsche, *Ber.*, 1914, **47**, 1108.
[6] Fieser and Hershberg, *J. Amer. Chem. Soc.*, 1936, **58**, 2314.
[7] Skraup and Schwamberger, *Annalen*, 1928, **462**, 148.
[8] *Org. Synth.*, 1933, **13**, 12.
[9] Barnett and Sanders, *J.*, 1933, 434.

TABLE 4. *Cyclisation of lactones* (I) *to acids* (III) *by method* (iii).

Lactone		Acids				
No.	g.	AcOH (ml.)	HCl (ml.)	Time (hr.)	M. p.[a]	Yield (%)
I*a*	0·2	5	5	2	255—256°	98
I*b*	0·2	5	5	0·3	255—256	95
I*c*	0·5	10	10	3	267—268[b]	80
I*d*	1	15	30	5	271—272	90
I*e*	0·5	10	10	2	231—232	100
I*f*	0·2	5	5	2	244—245	100

		Found (%)				Required (%)			
No.	Formula	C	H	OMe	Cl	C	H	OMe	Cl
I*a*	$C_{19}H_{14}O_5$	71·3	4·5	9·0	—	70·8	4·3	9·6	—
I*b*	$C_{19}H_{15}O_4Cl$	66·3	4·35	16·3	10·0	66·55	4·4	18·1	10·3
I*d*	$C_{19}H_{14}O_4$	74·1	4·6	—	—	74·5	4·6	—	—
I*e*	$C_{20}H_{18}O_5$	70·85	5·45	26·2	—	71·0	5·3	27·5	—
I*f*	$C_{20}H_{18}O_4$	74·6	5·95	19·4	—	74·5	5·6	19·25	—

[a] Cryst. from AcOH unless otherwise stated. [b] From aq. AcOH; Howell and Robertson [1] gave m. p. 265° (see Table 3).

6 : 7-*Dimethoxy*-1-*phenylnaphthalene* (III*c*; R = H).—1-*p*-Chlorophenyl-6 : 7-dimethoxynaphthalene (0·15 g.), tetralin (0·5 ml.), and 40% palladised charcoal (0·3 g.) were heated at 205—210° (nitrobenzene bath) for 3·5 hr.[4] The product was extracted with benzene and filtered from the catalyst. Recovery of the product and crystallisation from light petroleum (b. p. 40—60°) gave 6 : 7-dimethoxy-1-phenylnaphthalene in rosettes, m. p. 107—109°, undepressed on admixture with a specimen prepared by the decarboxylation of 6 : 7-dimethoxy-4-phenylnaphthalene-2-carboxylic acid [1] (III*c*; R = CO_2H) (Found: C, 81·3; H, 6·1; OMe, 23·7. Calc. for $C_{18}H_{16}O_2$: C, 81·8; H, 6·1; OMe, 23·5%).

6 : 7-*Methylenedioxy*-1-p-*tolylnaphthalene* (III*d*; R = H).—The acid (III*d*; R = CO_2H) (0·5) (Table 4) was similarly decarboxylated with copper-bronze (2 × 0·2 g.) in quinoline (4 ml.). The product (*ca.* 0·4 g.), on repeated crystallisation from light petroleum (b. p. 60—80°), gave 6 : 7-*methylenedioxy*-1-p-*tolylnaphthalene*, m. p. 121—122° (Found: C, 82·3; H, 5·4. $C_{18}H_{14}O_2$ requires C, 82·4; H, 5·3%).

Methyl 6 : 7-*Dimethoxy*-4-p-*methoxyphenylnaphthalene*-2-*carboxylate* (III*e*; R = CO_2Me).—*Method* (A). The acid (III*e*: R = CO_2H) (0·7 g.) was esterified by concentrated sulphuric acid (4 ml.) in boiling methanol (10 ml.) (4 hr.). The methyl ester (III*e*; R = CO_2Me) was obtained in colourless crystals (from methanol), m. p. and mixed m. p. with the product from method (i), 139—140°. *Method* (B). The acid (0·5 g.), dimethyl sulphate (0·75 g.), and potassium carbonate (2 g.) in acetone (20 ml.) were refluxed for 12 hr., then worked up as usual. The ester had m. p. and mixed m. p. 139—140°.

6 : 7-*Dimethoxy*-1-p-*methoxyphenylnaphthalene* (III*e*; R = H).—A stirred mixture of the acid (III*e*; R = CO_2H) (0·5 g.) and copper-bronze (0·4 g.) in quinoline (4 ml.) was heated on a sand-bath for 1 hr. and then worked up as usual. The brown semisolid product distilled at 170—175°/2 mm. (*ca.* 0·3 g.) and the solidified distillate crystallised from methanol, to give 6 : 7-*dimethoxy*-1-p-*methoxyphenylnaphthalene*, plates, m. p. 96—97° (Found: C, 77·3; H, 6·1; OMe, 31·4. $C_{19}H_{18}O_3$ requires C, 77·55; H, 6·1; OMe, 31·6%).

Methyl 6 : 7-*Dimethoxy*-4-p-*tolylnaphthalene*-2-*carboxylate* (III*f*; R = CO_2Me).—Prepared by either method, as above, from the acid, this ester had m. p. and mixed m. p. 146—147°.

6 : 7-*Dimethoxy*-1-p-*tolylnaphthalene* (III*f*; R = H).—Copper-bronze (0·2 g.) was added to a stirred solution of 6 : 7-dimethoxy-4-*p*-tolylnaphthalene-2-carboxylic acid (0·5 g.) in quinoline (4 ml.) and the whole was heated in an ethyl cinnamate bath (265—275°). A further amount of copper-bronze (0·2 g.) was then added, and heating and stirring were continued for further 2 hr. The product (0·2 g.) recrystallised from methanol, to give pale brown 6 : 7-*dimethoxy*-1-p-*tolylnaphthalene*, m. p. 98—99° (Found: C, 81·8; H, 6·5; OMe, 22·1. $C_{19}H_{18}O_2$ requires C, 82·0; H, 6·5; OMe, 22·3%).

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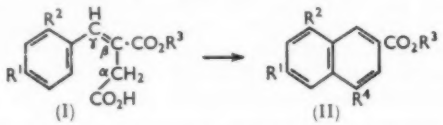
A'IN-SHAMS UNIVERSITY, CAIRO, EGYPT. [*Received, August 22nd,* 1958.]

208. *The Stobbe Condensation. Part I. The Cyclisation of Methyl Hydrogen* cis-γ-o-*Methoxyphenyl- and Methyl Hydrogen* cis-γ-p-*Methoxyphenyl-itaconate to the Corresponding Naphthalene Derivatives.*

By A. M. El-Abbady and Lanson S. El-Assal.

Methyl hydrogen *cis*-γ-*o*-methoxyphenyl- and methyl hydrogen *cis*-γ-*p*-methoxyphenyl-itaconate have been isolated on Stobbe condensation of *o*- and *p*-methoxybenzaldehyde with methyl succinate. They are cyclised by acetic anhydride and sodium acetate to methyl 4-acetoxy-8- and -6-methoxy-2-naphthoate which are converted into 1 : 5- and 1 : 7-dimethoxynaphthalene, respectively.

The *cis*-β-half esters, methyl hydrogen *cis*-γ-*o*- (I*a*; R^3 = Me) and *cis*-γ-*p*-methoxyphenyl-itaconate (I*b*; R^3 = Me) are obtained in about 76% yield by Stobbe condensation of *o*- and *p*-methoxybenzaldehyde, respectively, with dimethyl succinate and *tert.*-butyl alcoholic potassium *tert.*-butoxide.[1] Condensation with ethanolic sodium ethoxide gave inferior results.[2,3] The structure and the *cis*-configuration of the products were confirmed by their cyclisation with sodium acetate in acetic anhydride [3] to methyl 4-acetoxy-8- and -6-methoxy-2-naphthoate (II*a* and *b*; R^3 = Me, respectively) in nearly quantitative yield, and this provides a new route for synthesis of naphthalene derivatives.



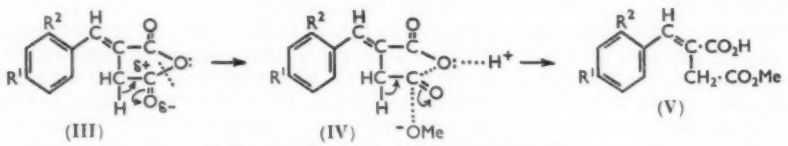
(I) (II)

	R^1	R^2	R^4
(I*a*)	H	OMe	—
(I*b*)	OMe	H	—
(II*a*)	H	OMe	OAc
(II*b*)	OMe	H	OAc

However, the parent itaconate (I; $R^1 = R^2 = H$, R^3 = Me) itself gave a very low yield, with much resin.

Alkaline hydrolysis of the acetoxy-esters gave 4-hydroxy-8- and -6-methoxy-2-naphthoic acid (as II), respectively. These phenolic acids were converted by methyl sulphate and potassium carbonate in acetone into the corresponding dimethoxy-esters which were hydrolysed to the dimethoxy-acids and then decarboxylated to give 1 : 5- and 1 : 7-dimethoxynaphthalene, respectively. The 1 : 5-compound was identical with an authentic specimen,[3a,4] but the 1 : 7-compound was an oil which was characterised as a dinitro-derivative.

Hydrolysis of the *cis*-β-half esters (I*a* and *b*; R^3 = Me) with boiling aqueous barium hydroxide gave the *cis*-itaconic acids, identical with those obtained by Baddar, El-Assal, Doss, and Shehab.[5] These were converted by acetyl chloride [2,3] into their *cis*-anhydrides



(III) (IV) (V)

a: R^1 = H, R^2 = OMe. *b*: R^1 = OMe, R^2 = H.

(III*a* and *b*, respectively). With boiling methanol [3b] these anhydrides gave the *cis*-α-half esters (V*a* and *b*) which were different from the *cis*-β-half esters (I*a* and *b*; R^3 = Me)

[1] Cf. Johnson and Daub, "Organic Reactions," J. Wiley and Sons Inc., 1951, Vol. VI, p. 1.
[2] Johnson *et al.*, *J. Amer. Chem. Soc.*, 1947, **69**, 74; 1950, **72**, 511.
[3] Baddar, El-Assal, and Baghos, *J.*, (*a*) 1955, 1714; (*b*) 1958, 986.
[4] Naylor and Gardner, *J. Amer. Chem. Soc.*, 1931, **53**, 4109.
[5] Baddar, El-Assal, Doss, and Shehab, *J.*, 1959, 1016.

obtained by the Stobbe condensation. This adds evidence for the structures of the *cis*-β-half esters (I).

It has been noted [3b, 6] that alcoholysis of anhydrides of type (III) always yields a half ester of type (V) and not that of type (I). This might be due to the attack of a proton on the cyclic oxygen atom of the anhydride, leading to a positive charge on the neighbouring carbon atom stabilised by hyperconjugation (cf. III); the anion MeO^- attacks this positive centre (see IV), which leads to the α-half ester (V).

Experimental

Methyl Hydrogen cis-γ-o-*Methoxyphenylitaconate* (I*a*; R^3 = Me).—A solution of *o*-methoxybenzaldehyde (13·6 g., 1 mol.) and methyl succinate (17·5 g., 1·2 mol.) in *tert.*-butyl alcohol (15 ml.) was added to a boiling solution of potassium *tert.*-butoxide [from metallic potassium (5·8 g.) in *tert.*-butyl alcohol (85 ml.)] during 15 min., and the whole refluxed for a further 45 min. The cold mixture was acidified (litmus) with concentrated hydrochloric acid. Evaporation under reduced pressure left a brown viscous oil which was treated with ice-water and extracted with ether. The ethereal solution was washed with water and repeatedly extracted with cold sodium hydrogen carbonate solution, then acidified. The product was filtered off, washed, dried (*ca.* 18·5 g.), and digested with boiling benzene, and the whole was filtered (residue *ca.* 1·6 g.). The benzene solution on concentration afforded a nearly colourless product which on repeated crystallisation from benzene gave *methyl hydrogen* cis-γ-o-*methoxyphenylitaconate* (*ca.* 13 g.), m. p. 138—140° (Found: C, 61·4; H, 5·6; OMe, 24·2. $C_{13}H_{14}O_5$ requires C, 62·4; H, 5·65; OMe, 24·8%. The low value for carbon is attributed to partial hydrolysis).

Evaporation of the benzene mother-liquor precipitated a semi-solid light brown product which is probably a mixture of the stereoisomeric half-esters of type (I).

Methyl 4-*Acetoxy*-8-*methoxy*-2-*naphthoate* (II*a*; R^3 = Me).—The above half ester (11 g.) and sodium acetate (3·5 g.) in acetic anhydride (50 ml.) were refluxed for 5 hr., then worked up as usual.[3] Evaporation left *methyl* 4-*acetoxy*-8-*methoxy*-2-*naphthoate* (*ca.* 11 g.), m. p. 124—127°, which after two crystallisations from benzene–light petroleum (b. p. 60—80°) formed needles, m. p. 128—129° (Found: C, 65·6; H, 5·2; OMe, 22·6. $C_{15}H_{14}O_5$ requires C, 65·7; H, 5·1; OMe, 22·6%).

This ester with 15% aqueous-alcoholic (v/v) potassium hydroxide (100 ml.) (2 hours' refluxing) gave pale-yellow 4-*hydroxy*-8-*methoxy*-2-*naphthoic acid* in crystals (*ca.* 7·5 g.), m. p. 259—260° (from acetic acid) (Found: C, 65·8; H, 4·7; OMe, 14·0. $C_{12}H_{10}O_4$ requires C, 66·05; H, 4·6; 2OMe, 14·2%).

Methyl 4 : 8-*Dimethoxy*-2-*naphthoate*.—The above phenolic acid (5 g.), dimethyl sulphate (14·5 g.), and anhydrous potassium carbonate (19 g.) in acetone (150 ml.) were refluxed for 12 hr., affording *methyl* 4 : 8-*dimethoxy*-2-*naphthoate* (5·3 g.), plates (from methanol), m. p. 107—108° (Found: C, 68·8; H, 5·7; OMe, 37·6. $C_{14}H_{14}O_4$ requires C, 68·3; H, 5·7; 3OMe, 37·8%). Hydrolysis of this (4 g.) with 15% aqueous-alcoholic (v/v) potassium hydroxide solution (50 ml.) (2 hours' refluxing) as above gave the *dimethoxy-acid*, m. p. 214—215° (from acetic acid) (Found: C, 66·8; H, 5·3; OMe, 25·8. $C_{13}H_{12}O_4$ requires C, 67·2; H, 5·2; 2OMe, 26·7%).

1 : 5-*Dimethoxynaphthalene*.—The preceding acid (0·5 g.) was refluxed in quinoline (5 ml.) with copper-bronze (0·8 g.) for 2·5 hr., and then worked up as usual. The product (0·3 g.) crystallised from benzene, to give 1 : 5-dimethoxynaphthalene, m. p. 183—184°, undepressed on admixture with an authentic specimen.[2a, 4]

Methyl Hydrogen cis-γ-p-*Methoxyphenylitaconate* (I*b*; R^3 = Me).—*p*-Methoxybenzaldehyde (13·6 g., 1 mol.) and methyl succinate (17·5 g., 1·2 mol.) in *tert.*-butyl alcohol (25 ml.) were added to a boiling solution of potassium *tert.*-butoxide [from metallic potassium (5·8 g.) and the alcohol (95 ml.)] during 30 min. and the whole was refluxed for a further 30 min., then worked up as described for the *o*-isomer. The solid product (*ca.* 19 g.) was digested in boiling benzene, and the solution was filtered from the insoluble residue (*ca.* 2 g.). The benzene solution on concentration afforded *methyl hydrogen* cis-γ-p-*methoxyphenylitaconate* which on repeated crystallisation from benzene had m. p. 119—120° (13 g.) (Found: C, 62·0; H, 5·85; OMe, 24·3. $C_{13}H_{14}O_5$ requires C, 62·4; H, 5·65; 2OMe, 24·8%).

Methyl 4-*Acetoxy*-6-*methoxy*-2-*naphthoate* (II*b*; R^3 = Me).—The preceding ester (5 g.) was

[6] Johnson and Goldman, *J. Amer. Chem. Soc.*, 1944, **66**, 1030.

cyclised with sodium acetate (1·7 g.) in boiling acetic anhydride (30 ml.) (6 hr.) in the usual manner. The *naphthoate* (*ca.* 5·4 g.), on crystallisation from benzene–light petroleum (b. p. 40—60°), had m. p. 125—126° (Found: C, 65·6; H, 5·0; OMe, 21·9. $C_{15}H_{14}O_5$ requires C, 65·7; H, 5·1; 2OMe, 22·6%).

Hydrolysis of this ester (II*b*; R^3 = Me, as for its isomer (50 ml.) (2 hours' refluxing) gave 4-*hydroxy*-6-*methoxy*-2-*naphthoic acid* (*ca.* 4·5 g.), m. p. 200—201° (decomp.) (from dilute acetic acid) (Found: 60·75; H, 5·3; OMe, 12·5. $C_{12}H_{10}O_4,H_2O$ requires C, 61·0; H, 5·1; 2OMe, 13·1%). The analytical result was the same even when the acid had been heated at 60—70°/4 mm. for 3 hr. When the acid was crystallised from glacial acetic acid, its solution gradually darkened and gave light-brown and violet crystals. The former had m. p. 252—254°, and on crystallisation from glacial acetic acid became heterogeneous. Therefore, the crude acid was used in the next experiment.

Methyl 4 : 6-*Dimethoxy*-2-*naphthoate*.—The preceding crude phenolic acid (4 g.), methyl sulphate (12 g.), potassium carbonate (15 g.), and acetone (100 ml.) were refluxed for 10 hr., then worked up as usual, giving *methyl* 4 : 6-*dimethoxy*-2-*naphthoate* (~4·4 g.) in needles (from methanol), m. p. 104—105° (Found: C, 68·5; H, 5·9; OMe, 36·9. $C_{14}H_{14}O_4$ requires C, 68·3; H, 5·7; 3OMe, 37·8%). Hydrolysis of this (3 g.) with 15% aqueous-alcoholic (v/v) potassium hydroxide solution (50 ml.) gave the *dimethoxy-acid* (~2·8 g.), m. p. 262—263° (Found: C, 67·15; H, 5·3; OMe, 26·8. $C_{13}H_{12}O_4$ requires C, 67·2; H, 5·2; 2OMe, 26·7%).

1 : 7-*Dimethoxynaphthalene*.—The preceding acid (0·7 g.) and copper-bronze (0·5 g.) in quinoline (8 ml.) were heated at 205—210° (nitrobenzene-bath) for 1 hr. Further copper-bronze (0·5 g.) was added during a further hour with continuous heating and stirring, then the whole was worked up in the usual manner, affording a viscous brown oil. This oil was extracted with light petroleum (b. p. 40—60°), and the solution filtered from resin. Removal of the solvent gave 1 : 7-dimethoxynaphthalene as a pale brown oil. Nitric acid (*d* 1·42; 0·6 ml.) in acetic acid (5 ml.) was added to a stirred solution of the oil (0·55 g.) in acetic acid (10 ml.) during 30 min. at 30—35°, and then left overnight.[3b] The precipitated crystals (*ca.* 0·4 g.) recrystallised from acetic acid, to give a pale yellow *dinitro-derivative*, m. p. 212—213° (Found: C, 51·8; H, 3·85; N, 10·15; OMe, 22·1. $C_{12}H_{10}O_6N_2$ requires C, 51·8; H, 3·6; N, 10·1; 2OMe, 22·3%).

cis-*γ*-o-*Methoxyphenylitaconic Acid*.—The *cis*-β-half ester (I*a*; R^3 = Me) (6 g.) was hydrolysed with a concentrated barium hydroxide solution (100 ml.) (2 hours' refluxing), and the precipitated barium salt was filtered off, washed with water and with alcohol, and dried. Acidification with dilute hydrochloric acid liberated an acid which was filtered off, washed, and dried (*ca.* 6 g.). Crystallisation from dilute acetic acid gave *cis-γ-o*-methoxyphenylitaconic acid in pale yellow crystals,[5] m. p. 210—211°.

cis-*γ*-o-*Methoxyphenylitaconic Anhydride* (III*a*).—The above acid (5 g.) was boiled with acetyl chloride (6 ml.) for 2 hr. After evaporation the residue recrystallised from benzene, to give the *anhydride* (*ca.* 4·2 g.) in needles, m. p. 132—133° (Found: C, 66·0; H, 4·7; OMe, 13·9. $C_{13}H_{10}O_4$ requires C, 66·05; H, 4·6; 2OMe, 14·2%).

α-*Methyl* β-*Hydrogen* cis-*γ*-o-*Methoxyphenylitaconate* (V*a*).—The anhydride (1 g.) was refluxed in methanol (20 ml.) for 3 hr. Evaporation and crystallisation of the residue (1 g.) from benzene–light petroleum (b. p. 80—100°) gave α-*methyl* β-*hydrogen* cis-*γ*-o-*methoxyphenylitaconate*[3b] in needles, m. p. 128—130°, depressed on admixture with the isomeric ester (Found: C, 62·6; H, 5·75; OMe, 24·2. $C_{13}H_{14}O_5$ requires C, 62·4; H, 5·6; 2OMe, 24·8%).

cis-*γ-p-Methoxyphenylitaconic Acid* (I*b*; R^3 = H).—The β-half-ester was refluxed with concentrated barium hydroxide solution (200 ml.) for 6 hr., then worked up as described for its *o*-isomer. The *cis-γ-p*-methoxyphenylitaconic acid was obtained in lemon-yellow crystals,[5] m. p. 202—203°.

cis-*γ*-p-*Methoxyphenylitaconic Anhydride* (III*b*).—The preceding acid (I*b*; R^3 = H) (0·5 g.) with acetyl chloride (15 ml.) (3 hours' refluxing) gave the *itaconic anhydride* (*ca.* 0·4 g.), flakes (from benzene), m. p. 166—167° (Found: 66·1; H, 4·7; OMe, 13·65%).

α-*Methyl* β-*Hydrogen* cis-*γ*-p-*Methoxyphenylitaconate* (V*b*).—The anhydride (III*b*) (*ca.* 0·5 g.) in methanol (30 ml.) gave, as in the preceding case, α-*methyl* β-*hydrogen* γ-p-*methoxyphenylitaconate* (~0·5 g.), needles [from benzene–light petroleum (b. p. 50—60°)], m. p. 139—140°, depressed on admixture with the β-half-ester (Found: C, 62·3; H, 5·7; OMe, 24·1%).

The authors thank Professor F. G. Baddar for facilities.

A'IN-SHAMS UNIVERSITY, CAIRO, EGYPT. [*Received, August 22nd,* 1958.]

209. *Phenylpropiolic Acids. Part VI.* The Cyclisation of Dissimilarly Substituted Phenylpropiolic Anhydrides to the Corresponding 1-Phenylnaphthalenes.*

By F. G. Baddar, Lanson S. El-Assal, and N. A. Doss.

Dissimilarly substituted phenylpropiolic anhydrides have been prepared but not isolated. They cyclise directly to a mixture of isomeric 1-phenylnaphthalene-2 : 3-dicarboxylic anhydrides. Their derived dibasic acids give 1-phenylnaphthalenes on decarboxylation.

The present investigation is an extension of a previous study by Baddar and El-Assal [1] who suggested the formation of dissimilarly substituted phenylpropiolic anhydrides by the interaction between equimolecular amounts of arylpropioloyl chloride with arylpropiolic acids in benzene. These anhydrides cyclise readily under the conditions of the reaction to the corresponding 1-phenylnaphthalenes, and since the two aryl radicals of the arylpropiolic anhydrides are dissimilar, the product was a mixture of two isomeric 1-phenylnaphthalene derivatives. The aim was to study the effect of different substituents on the mode of cyclisation of these anhydrides.

When *p*-chlorophenylpropiolic acid was self-condensed it gave 7-chloro-1-*p*-chlorophenylnaphthalene-2 : 3-dicarboxylic anhydride (Ia) identical with a specimen prepared by the Stobbe condensation.[2] This anhydride with aluminium chloride in nitrobenzene gave 3′ : 7-dichloro-3 : 4-benzofluorenone-1-carboxylic acid (IIa); an isomeric anhydride (Ib) failed to do so.[3] Since 5-methoxy-1-*o*-methoxyphenyl-[4] (Ic) and 5-methyl-1-*o*-tolylnaphthalene-2 : 3-dicarboxylic anhydride [3] (Id) are readily converted into their corresponding benzofluorenones (II), it appears that the failure of the chloro-compound (Ib) to do so is due to the interaction between the bulky chlorine atom and the 8-hydrogen atom, which prevents the required coplanarity.

When *o*-chlorophenylpropioloyl chloride was refluxed with *o*-methoxyphenylpropiolic acid in benzene, a mixture of anhydrides was obtained from which 1-*o*-chlorophenyl-5-methoxy- (Ie) and 5-chloro-1-*o*-methoxy-phenylnaphthalene-2 : 3-dicarboxylic anhydrides (If) were isolated. The structure of the latter was established by decarboxylating its derived dibasic acid to 5-chloro-1-*o*-methoxyphenylnaphthalene (IVf), identical with a specimen prepared by heating 5-chloro-1 : 2 : 3 : 4-tetrahydro-1-*o*-methoxyphenyl-1-naphthol (Vf) with selenium. This tertiary alcohol was prepared from 5-chloro-1-tetralone in the usual way, this in turn being prepared by reduction of *o*-chlorocinnamic acid with lithium aluminium hydride to 3-*o*-chlorophenylpropan-1-ol which was converted into the bromide and then by a Grignard reaction into γ-*o*-chlorophenylbutyric acid which was cyclised. The same two isomeric anhydrides (Ie and f) were obtained by cyclisation of dissimilarly substituted dibenzylidenesuccinic anhydrides.[2]

When *o*-chlorophenylpropioloyl chloride was refluxed with *o*-tolylpropiolic acid in benzene, it gave the anhydrides (Ig and h) which were isolated and identified, together with (Id).[3]

Interaction of *o*-chlorophenylpropioloyl chloride (or acid) and *p*-chlorophenylpropiolic acid (or chloride) gave a mixture of anhydrides from which 7-chloro-1-*p*-chlorophenylnaphthalene-2 : 3-dicarboxylic anhydride (Ia) was isolated as the main product. The product also contained a small quantity of 7-chloro-1-*o*-chlorophenylnaphthalene-2 : 3-dicarboxylic anhydride (Ii).

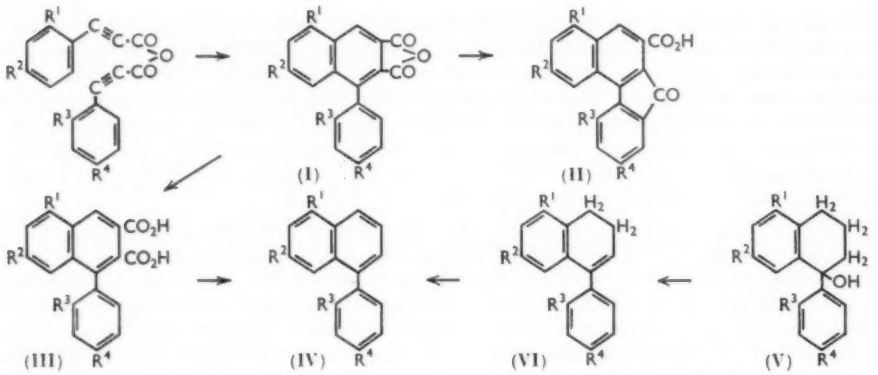
* Part V, *J.*, 1955, 465.

[1] Baddar and El-Assal, *J.*, 1951, 1844.
[2] Baddar, El-Assal, Doss, and Shehab, *J.*, 1959, 1016.
[3] Baddar, El-Assal, and Doss, *J.*, 1955, 461.
[4] Baddar, *J.*, 1947, 224.

XUM

Refluxing *o*-chlorophenylpropioloyl chloride with severally phenyl-, *p*-methoxyphenyl-, *p*-tolyl-, and *p*-chlorophenyl-propiolic acid gave 1-phenyl-, 7-methoxy-1-*p*-methoxyphenyl-,[5] 7-methyl-1-*p*-tolyl-,[3] and 7-chloro-1-*p*-chlorophenyl-naphthalene-2 : 3-dicarboxylic anhydride, respectively, as the only anhydrides isolated. However, *p*-chlorophenylpropioloyl chloride with phenylpropiolic acid as usual gave a mixture of anhydrides from which the two anhydrides (Ij and k) were isolated.

Condensation of *p*-methoxyphenylpropioloyl chloride with phenylpropiolic acid in the usual manner gave a mixture of anhydrides from which were isolated the two compounds (Il and m), obtained also by cyclisation of the dissimilarly substituted dibenzylidenesuccinic anhydride prepared by a two-step Stobbe condensation.[2]



	R^1	R^2	R^3	R^4
a	H	Cl	H	Cl
b	Cl	H	Cl	H
c	OMe	H	OMe	H
d	Me	H	Me	H
e	OMe	H	Cl	H
f	Cl	H	OMe	H
g	Cl	H	Me	H

	R^1	R^2	R^3	R^4
h	Me	H	Cl	H
i	H	Cl	Cl	H
j	H	Cl	H	H
k	H	H	H	Cl
l	H	OMe	H	H
m	H	H	H	OMe

The structure of the anhydrides (Ig, j, and m) was established by decarboxylating the derived dibasic acid to the corresponding 1-phenylnaphthalene derivatives, which were identical with authentic specimens prepared by the Grignard reaction as usual.[1] However, the structure of the anhydrides (Ie, h, and i) rested on their failure to give a 3 : 4-benzofluorenone derivative, which indicates the presence of the chlorine atom in the 2′-position.

The preferential formation of a 1-phenylnaphthalene-2 : 3-dicarboxylic anhydride resulting from the self-condensation of the unsubstituted or the *p*-substituted phenylpropiolic acid, when one of the reactants is *o*-chlorophenylpropiolic acid or its acid chloride, may be due either to the steric effect of the bulky *o*-chlorine atom or to the relative stability of the acid chloride.

However, most of the above results can be interpreted by the mechanism put forward by Baddar and El-Assal.[1]

Experimental

p-Chlorocinnamic Acid.—This was prepared in the usual manner [3] from *p*-chlorobenzaldehyde (25 g.), malonic acid (22·2 g.), ethanol (50 ml.), and pyridine (3·1 ml.). The product (26 g.), crystallised from ethanol, had m. p. 249—250° (cf. Skraup and Beng,[6a] and Gabriel and Herzberg,[6b] give m. p. 240—242°).

[5] Baddar and El-Assal, *J.*, 1948, 1267.
[6] (*a*) Skraup and Beng, *Ber.*, 1927, **60**, 946; (*b*) Gabriel and Herzberg, *Ber.*, 1883, **16**, 203.

αβ-*Dibromo*-β-p-*chlorophenylpropionic Acid*.—The above cinnamic acid (10 g.) in acetic acid (15 ml. was treated with bromine (3 ml.) in acetic acid (15 ml.) on a boiling-water bath for 1 hr. Dilution with water precipitated αβ-dibromo-β-*p*-chlorophenylpropionic acid (~ 18 g.), m. p. 194—195° (from benzene) (Found: Halogen, 57·3. Calc. for $C_9H_7O_2ClBr_2$: Halogen, 57·1%). Reich *et al.*[7] give m. p. 187°.

p-*Chlorophenylpropiolic Acid*.—The dibromo-acid (25 g.) in 25% methanolic potassium hydroxide (100 ml.) gave (cf. refs. 8 and 3) *p*-chlorophenylpropiolic acid (*ca.* 13 g.), m. p. 192—193° (from benzene) (Found: Cl, 19·4. Calc. for $C_9H_5O_2Cl$: Cl, 19·7%) (cf. Newman and Merrill [9]).

7-*Chloro*-1-p-*chlorophenylnaphthalene*-2 : 3-*dicarboxylic Anhydride* (Ia).—*p*-Chlorophenylpropiolic acid (5 g.) was refluxed with acetic anhydride (20 ml.) for 5 hr. The product (*ca.* 2·5 g.) was repeatedly crystallised from benzene, to give the *anhydride*, m. p. 266—267° (Found: C, 62·6; H, 2·4; Cl, 20·8. $C_{18}H_8O_3Cl_2$ requires C, 63·0; H, 2·3; Cl, 20·7%).

3′ : 7-*Dichloro*-3 : 4-*benzofluorenone*-1-*carboxylic Acid* (IIa).—The anhydride (3 g.) was heated with anhydrous aluminium chloride (15 g.) and nitrobenzene (50 ml.) on a boiling-water bath for 4 hr. with stirring. Nitrobenzene was removed with steam, and the product extracted with ammonia. The insoluble ammonium salt was acidified; the liberated *acid* (2·9 g.) crystallised from benzene or nitrobenzene in deep-red needles, m. p. 317—318° (Found: C, 62·7; H, 2·3; Cl, 20·5. $C_{18}H_8O_3Cl_2$ requires C, 63·0; H, 2·3; Cl, 20·7%).

p-*Chlorophenylpropioloyl Chloride*.—This *chloride* was prepared from the acid (18 g.) and thionyl chloride (50 ml.) (2 hours' refluxing) and distilled at 100—105°/1 mm., then crystallised from light petroleum (b. p. 40—60°); it had m. p. 68—69° (Found: Cl, 35·7. $C_9H_4OCl_2$ requires Cl, 35·7%).

Action of p-*Chlorophenylpropioloyl Chloride on* o-*Chlorophenylpropiolic Acid*.—A mixture of acid (9 g.) and freshly prepared chloride (9·9 g.) in dry benzene (100 ml.) was refluxed for 36 hr. Removal of benzene left a solid (A) which was washed with ether, then repeatedly crystallised from benzene, to give the anhydride (Ia), m. p. and mixed 266—267°. The product separating from the benzene mother-liquor on storage was fractionally crystallised from the same solvent to give the *anhydride* (Ii), m. p. 196—197°, depressed on admixture with either anhydride (Ia or b) (Found: C, 62·6; H, 2·6; Cl, 20·6. $C_{18}H_8O_3Cl_2$ requires C, 63·0; H, 2·3; Cl, 20·7%). When the anhydride (Ii) (0·5 g.) had been heated for 4 hr. at 40° with aluminium chloride (2·5 g.) in nitrobenzene (10 ml.), it was recovered unchanged.

Action of o-*Chlorophenylpropioloyl Chloride on* o-*Methoxyphenylpropiolic Acid*.—Freshly prepared *o*-chlorophenylpropioloyl chloride (9·9 g.) and *o*-methoxyphenylpropiolic acid [4] (8·8 g.) in benzene (100 ml.) were refluxed for 30 hr. The product (*ca.* 7·5 g.) precipitated on cooling (m. p. 240—246°) gave, on repeated crystallisation from benzene, 1-o-*chlorophenyl*-5-*methoxynaphthalene*-2 : 3-*dicarboxylic anhydride* (Ie) in lemon-yellow crystals (*ca.* 1·5 g.), m. p. 251—252°, depressed on admixture with the anhydride (Ic or b) (Found: C, 67·2; H, 2·95; Cl, 10·5. $C_{19}H_{11}O_4Cl$ requires C, 67·35; H, 2·95; Cl, 10·5%).

The benzene mother-liquor was evaporated and the oily residue diluted with ether (100 ml.) and kept overnight. The precipitated product (*ca.* 5 g.), m. p. 220—224°, was fractionally crystallised from benzene. The first fraction was identified as the previous anhydride. The benzene mother-liquor afforded on slow evaporation crystals, which on repeated crystallisation from the same solvent gave 5-*chloro*-1-o-*methoxyphenylnaphthalene*-2 : 3-*dicarboxylic anhydride* (If), m. p. 198—199° (*ca.* 0·6 g.), depressed on admixture with the above isomeric anhydride and with anhydride (Ib) (Found: C, 67·3; H, 3·1; Cl, 10·4%).

3-o-*Chlorophenylpropan*-1-*ol*.—*o*-Chlorocinnamic acid (91 g.) was added during 1 hr. to a stirred suspension of lithium aluminium hydride (40 g.) in ether (100 ml.) at 0°. Then the mixture was refluxed for an hour and worked up as usual. The product was distilled, to give 3-o-*chlorophenylpropan*-1-*ol*, b. p. 100—101°/2 mm. (*ca.* 82 g.), n_D^{25} 1·5390 (Found: C, 63·7; H, 6·7; Cl, 20·6. $C_9H_{11}OCl$ requires C, 63·3; H, 6·45; Cl, 20·8%).

1-*Bromo*-3-o-*chlorophenylpropane*.—3-*o*-Chlorophenylpropan-1-ol (75 g.) and 40% hydrobromic acid (200 ml.) were refluxed for 5 hr., then worked up as usual and distilled, to give 1-*bromo*-3-o-*chlorophenylpropane* (*ca.* 70 g.), b. p. 95—96°/2 mm. (Found: C, 46·4; H, 4·45; Halogen, 49·1. $C_9H_{10}ClBr$ requires C, 46·25; H, 4·3; Halogen, 49·4%).

[7] Reich, Araus, Potok, and Tempel, *Helv. Chim. Acta*, 1920, **3**, 793.
[8] Reimer, *J. Amer. Chem. Soc.*, 1942, **64**, 2510.
[9] Newman and Merrill, *ibid.*, 1955, **77**, 5549.

XUM

γ-o-Chlorophenylbutyric Acid.—The Grignard reagent [from 1-bromo-3-*o*-chlorophenylpropane (50·5 g.) and magnesium (5·3 g.) in ether (200 ml.)] was rapidly added to solid carbon dioxide, left for 4 hr., and worked up as usual. The *acid* produced crystallised from light petroleum (b. p. 60—80°), then having m. p. 94—95° (*ca.* 20 g.) (Found: C, 60·3; H, 5·6; Cl, 17·8. $C_{10}H_{11}O_2Cl$ requires C, 60·45; H, 5·5; Cl, 17·9%).

5-*Chloro*-1-*tetralone.*—*γ-o*-Chlorophenylbutyric acid (15 g.) was kept in anhydrous hydrogen fluoride (120 ml.) for 2 days, then worked up as usual. The *product*, crystallised from light petroleum (b. p. 40—60°), had m. p. 67·5—68·5° (*ca.* 7 g.) (Found: C, 66·4; H, 5·2; Cl, 19·4. $C_{10}H_9OCl$ requires C, 66·5; H, 5·0; Cl, 19·7%). Its 2 : 4-*dinitrophenylhydrazone* formed deep-red needles (from benzene), m. p. 259—260° (Found: C, 53·6; H, 3·8; N, 15·9. $C_{16}H_{13}O_4N_2Cl$ requires C, 53·3; H, 3·7; N, 15·5%).

5-*Chloro*-1 : 2 : 3 : 4-*tetrahydro*-1-*o*-*methoxyphenyl*-1-*naphthol* (Vf).—5-Chloro-1-tetralone (5 g.) in dry ether (50 ml.) was added during 30 min. to a stirred solution of *o*-methoxyphenylmagnesium bromide [from *o*-bromoanisole (7·2 g.) and magnesium (1·4 g.) in ether (50 ml.)]. The mixture was left overnight and worked up as described by Baddar and El-Assal.[5] The product was distilled and the fraction boiling at 170—175°/2 mm. (*ca.* 7 g.) was collected, then crystallised from methanol to give the *tetralol*, m. p. 134—135° (Found: C, 70·8; H, 6·0; Cl, 12·2. $C_{17}H_{17}O_2Cl$ requires C, 70·7; H, 6·0; Cl, 12·3%). The presence of the hydroxyl group was confirmed by the infrared spectrum.

5-*Chloro*-1-*o*-*methoxyphenylnaphthalene* (IVf).—(i) The above tertiary alcohol (1 g.) and selenium powder (0·7 g.) were heated at 300—310° for 2 hr. The product was purified by chromatography over alumina [light petroleum (b. p. <40°) was used as a developer]. On repeated crystallisation from methanol, 5-*chloro*-1-*o*-*methoxyphenylnaphthalene*, m. p. 96—97°, was obtained (Found: C, 75·7; H, 4·7; Cl, 13·0. $C_{17}H_{13}OCl$ requires C, 76·0; H, 4·8; Cl, 13·2%). (ii) The acid (IIIf) (0·5 g.) [prepared from the anhydride] was heated in quinoline (4 ml.) with copper-bronze (0·2 g.) at 205—210° (nitrobenzene-bath) for 30 min. with stirring. More copper-bronze (0·2 g.) was added in portions during 2 hr., stirring and heating were continued for a further hour, and the whole was worked up as usual. The product was purified by distillation (b. p. 180—190°/2 mm.), followed by crystallisation from methanol, to give 5-chloro-1-*o*-methoxyphenylnaphthalene (IVf) (0·25 g.), m. p. 96—97°, undepressed on admixture with a specimen prepared by method (i) (Found: C, 76·0; H, 5·0; Cl, 13·1%).

Action of o-Chlorophenylpropioloyl Chloride on o-Tolylpropiolic Acid.—Freshly prepared *o*-chlorophenylpropioloyl chloride (9·9 g.) and *o*-tolylpropiolic acid (8 g.) in benzene (100 ml.) were refluxed for 32 hr. Removal of benzene left an oil which was treated with dry ether (100 ml.) and left overnight. The precipitated crystals were washed with ether (*ca.* 8 g.; m. p. 165—175°). Crystallisation of this product (5 g.) from benzene gave 5-*chloro*-1-*o*-*tolylnaphthalene*-2 : 3-*dicarboxylic anhydride* (Ig) (*ca.* 1·5 g.), m. p. 182—182·5°, depressed on admixture with anhydride [2] (Ib) (Found: C, 71·1; H, 3·65; Cl, 10·4. $C_{19}H_{11}O_3Cl$ requires C, 70·7; H, 3·4; Cl, 11·0%). The benzene mother-liquor yielded on storage another fraction, which after repeated crystallisation from benzene gave 5-methyl-1-*o*-tolylnaphthalene-2 : 3-dicarboxylic anhydride [3] (Id) (*ca.* 0·7 g.), m. p. and mixed m. p. 162—163°. Attempts to isolate the anhydride (Ih) from the product were unsuccessful. However, its presence was inferred from the following evidence:

A finely powdered mixture of the product (2 g.) from the above experiment with aluminium chloride (10 g.) was added during 10 min. to stirred nitrobenzene (20 ml.) so that the temperature did not rise above 40—50°. The mixture was left for 3 days at room temperature with occasional stirring and warming to 50°, then worked up as usual.[3] Acidification of the clear ammoniacal extract precipitated a mixture of acids which was filtered off and dried (*ca.* 2 g.). It was extracted with ether, and the colourless ethereal solution was filtered from the insoluble red product. Distillation of ether left a residue (*ca.* 0·17 g.) which was dissolved in chloroform and run through 9 : 1 silica–calcite, with 1 : 1 ether–light petroleum (b. p. 50—60°) as developer. The product (*ca.* 0·15 g.) was heated with acetyl chloride (1 ml.), then crystallised from benzene, to give 1-*o*-*chlorophenyl*-5-*methylnaphthalene*-2 : 3-*dicarboxylic anhydride* (*ca.* 0·1 g.), m. p. 244—246° depressed on admixture with the anhydride (Ig, d, or b) (Found: C, 71·0; H, 3·7; Cl, 10·6. $C_{19}H_{11}O_3Cl$ requires C, 70·7; H, 3·4; Cl, 11·0%). The red-brown ether-insoluble residue was fractionally crystallised from benzene. The first fraction, m. p. 218—220°, gave on crystallisation from the same solvent 1′-*chloro*-5-*methyl*-3 : 4-*benzofluorenone*-1-*carboxylic acid* (IIg) (*ca.* 0·6 g.), depressed on admixture with the acid (IId) (Found: C, 71·3; H, 3·6; Cl, 10·2.

$C_{19}H_{11}O_3Cl$ requires C, 70·7; H, 3·4; Cl, 11·0%). The second fraction, m. p. 230—234°, on repeated crystallisation from benzene gave this acid (IId) (*ca.* 0·6 g.), m. p. 236—238°, undepressed on admixture with an authentic specimen.[3]

8-*Chloro*-1 : 2-*dihydro*-4-o-*tolylnaphthalene* (VIf).—5-Chloro-1-tetralone (5 g.) in dry ether (50 ml.) was added dropwise to ethereal *o*-tolylmagnesium bromide [from *o*-bromotoluene (7 g.) and magnesium (1·4 g.)] in ether (50 ml.) during 30 min. with occasional stirring, left overnight, then worked up as usual.[1,5] The *product* was fractionated (b. p. 160—165/2 mm.; 6·5 g.), triturated with ether, then crystallised from methanol; it had m. p. 92—93° (Found: C, 79·9; H, 6·0; Cl, 13·7. $C_{17}H_{15}Cl$ requires C, 80·15; H, 6·0; Cl, 13·9%).

1-*Chloro*-5-o-*tolylnaphthalene* (IVg).—(i) The dihydro-compound (VIf) (1 g.) and selenium powder (0·7 g.) were heated at 300—310° for 3 hr. The product (0·7 g.) was chromatographed over alumina, then distilled (b. p. 170—180°/3 mm.). Nitration [10] gave an inseparable mixture. (ii) The acid (IIIg) (0·5 g.) and copper-bronze (0·4 g.) in quinoline (4 ml.) were treated as described for the decarboxylation above. The product was chromatographed, then distilled in a vacuum (b. p. 160—180°/2 mm.). The infrared spectra of this compound and that obtained by the previous method were identical. The identity of both products was also established by dehalogenation to the same 1-*o*-tolylnaphthalene (see next experiment).

1-o-*Tolylnaphthalene*.—(i) 1 : 2-Dihydro-4-*o*-tolylnaphthalene (0·5 g.) and 10% palladised charcoal (0·05 g.) were heated at 200—210° for 1 hr. The product, crystallised from methanol, gave 1-o-*tolylnaphthalene*, m. p. 72—73° (*ca.* 0·4 g.) (Found: C, 93·5; H, 6·65. $C_{17}H_{14}$ requires C, 93·4; H, 6·6%). (ii) 1-Chloro-5-*o*-tolylnaphthalene (0·5 g.) (obtained by the above two methods), tetralin (0·7 ml.), and 10% palladised charcoal (0·05 g.) were heated at 200—210°, then worked up as described in method (i). Crystallisation from methanol gave 1-*o*-tolylnaphthalene, m. p. and mixed m. p. 72—73° (Found: C, 93·6; H, 6·7%).

Action of o-*Chlorophenylpropioloyl Chloride on Phenyl-*, p-*Methoxyphenyl-*, p-*Tolyl-, and* p-*Chlorophenyl-propiolic Acid*.—A mixture from freshly prepared *o*-chlorophenylpropioloyl chloride [1,3] (19·9 g.) and phenylpropiolic acid (14·6 g.) in dry benzene (200 ml.) was worked up as usual after 32 hours' refluxing. The semi-solid product was triturated with ether (100 ml.), then crystallised from benzene to give 1-phenylnaphthalene-2 : 3-dicarboxylic anhydride (I) in pale-yellow crystals (*ca.* 10 g.), m. p. and mixed m. p. 252—253°. The ethereal mother-liquor gave, overnight, another crop (*ca.* 2·7 g.) of the same product.

A mixture from the same acid chloride (19·9 g.) and *p*-methoxyphenylpropiolic acid (17·6 g.) in benzene (200 ml.) was similarly worked up. The solid product (7·5 g.) precipitated from ether crystallised from benzene, to give 7-methoxy-1-*p*-methoxyphenylnaphthalene-2 : 3-dicarboxylic anhydride, m. p. and mixed m. p. 216—217°.[5] Unchanged *p*-methoxyphenylpropiolic acid [5] (*ca.* 0·5 g.) was recovered from the ethereal mother-liquor.

A mixture from the same acid chloride (19·9 g.) and *p*-tolylpropiolic acid (16 g.) in benzene (200 ml.), when similarly worked up, gave a solid (*ca.* 4 g.) after trituration with ether. This on crystallisation from benzene gave 7-methyl-1-*p*-tolylnaphthalene-2 : 3-dicarboxylic anhydride [3] in pale-yellow crystals (*ca.* 3·5 g.), m. p. and mixed m. p. 267—268°.

Similarly, a mixture from the above acid chloride (19·9 g.) and *p*-chlorophenylpropiolic acid (18 g.) in benzene (200 ml.) gave *p*-chlorophenylpropiolic acid (*ca.* 6·5 g.) as the first crop. Evaporation of the benzene mother-liquor left a viscous oil which on trituration with ether and then crystallisation from benzene gave the anhydride (Ia) (*ca.* 1·5 g.), m. p. and mixed m. p. 266—267°. Another fraction of the same anhydride (*ca.* 6·5 g.) was obtained on storage.

Action of p-*Chlorophenylpropioloyl Chloride on Phenylpropiolic Acid*.—Freshly prepared *p*-chlorophenylpropioloyl chloride (3·2 g.), phenylpropiolic acid (2·3 g.), and dry benzene (80 ml.) were refluxed for 35 hr. The precipitated product was filtered off and thoroughly washed with ether (*ca.* 1·5 g.). Repeated crystallisation from benzene gave the *anhydride* (Ij), m. p. 251—252°, depressed on admixture with a specimen of anhydride (Ia) or 1-phenylnaphthalene-2 : 3-dicarboxylic anhydride (Found: C, 70·0; H, 3·0; Cl, 11·3. $C_{18}H_9O_3Cl$ requires C, 70·0; H, 2·9; Cl, 11·6%).

The original benzene mother-liquor was concentrated and on storage yielded another fraction (colourless) which was filtered off and washed with ether. On repeated crystallisation from benzene this gave the *anhydride* (Ik) (*ca.* 0·4 g.), m. p. 210—212°, depressed on admixture with the preceding two anhydrides or (Ia) (Found: C, 69·8; H, 2·8; Cl, 11·4%).

[10] Baddar, El-Assal, and Gindy, *J.*, 1948, 1270.

7-*Chloro*-1-*tetralone*.—Freshly distilled γ-*p*-chlorophenylbutyric acid [11] (40 g.) was left in anhydrous hydrogen fluoride (200 ml.) overnight, then worked up as described for the 5-chloro-derivative. The product (*ca.* 30 g.) was distilled (b. p. 150—155°/5 mm.), then crystallised from light petroleum (b. p. 55—65°), to give 7-chloro-1-tetralone, m. p. 94—95° (*ca.* 26 g.) (von Braun [12] gave m. p. 94° and Schroeter,[13] m. p. 96—97°) (Found: C, 66·7; H, 5·2; Cl, 19·5. Calc. for $C_{10}H_9OCl$: C, 66·5; H, 5·0; Cl, 19·7%).

7-*Chloro*-1 : 2 : 3 : 4-*tetrahydro*-1-*phenyl*-1-*naphthol* (Vj).—7-Chloro-1-tetralone (9 g.) in ether (40 ml.) was gradually added to phenylmagnesium bromide [from bromobenzene (12 g.) and magnesium (1·8 g.) in ether (80 ml.)], then worked up as usual. The product (*ca.* 14 g.) was fractionally distilled (b. p. 175—180°/2 mm.), then repeatedly crystallised from methanol to give the *tetralol*, m. p. 81—82° (*ca.* 10 g.) (Found: C, 74·2; H, 5·7; Cl, 13·4. $C_{16}H_{15}OCl$ requires C, 74·3; H, 5·8; Cl, 13·7%). The structure of this tertiary alcohol was confirmed by its infrared spectrum.

7-*Chloro*-1-*phenylnaphthalene* (IVj).—(i) The above tertiary alcohol (3 g.) and selenium powder (2·5 g.) were heated at 320—330° for 3 hr., then worked up as usual. 7-*Chloro*-1-*phenylnaphthalene* (*ca.* 1·5 g.) had m. p. 77—78° (from methanol) (Found: C, 80·2; H, 4·7; Cl, 14·6. $C_{16}H_{11}Cl$ requires C, 80·5; H, 4·6; Cl, 14·8%). (ii) 7-Chloro-1-phenylnaphthalene-2 : 3-dicarboxylic acid (0·3 g.) (obtained from the anhydride as usual) was decarboxylated with copper-bronze (0·2 g.) in quinoline (5 ml.) as usual. The product was distilled (b. p. 150—155°/3 mm.; 0·2 g.), then crystallised from methanol to give 7-chloro-1-phenylnaphthalene, m. p. and mixed m. p. 77—78° (Found: C, 79·85; H, 4·6; Cl, 14·2%).

p-*Methoxyphenylpropioloyl Chloride*.—A mixture of *p*-methoxyphenylpropiolic acid [5] (3·6 g.) and thionyl chloride (3·5 ml.) was left overnight at 25—30°, then distilled (b. p. 150—160°/2 mm.) to give the *chloride* as a lemon-yellow oil (Found: Cl, 18·6. $C_{10}H_7O_2Cl$ requires Cl, 18·25%).

Action of p-*Methoxyphenylpropioloyl Chloride on Phenylpropiolic Acid*.—Freshly prepared *p*-methoxyphenylpropioloyl chloride (5·4 g.) and phenylpropiolic acid (4·5 g.) in benzene (80 ml.) were refluxed for 30 hr. The crystalline product was filtered off, and washed with ether. On repeated crystallisation from benzene, 1-p-*methoxyphenylnaphthalene*-2 : 3-*dicarboxylic anhydride* (Im) was obtained in lemon-yellow crystals (*ca.* 1·4 g.), m. p. 261—262°, depressed on admixture with 7-methoxy-1-*p*-methoxyphenyl- [5] or 1-phenyl-naphthalene-2 : 3-dicarboxylic anhydride (Found: C, 74·8; H, 4·2; OMe, 8·7. $C_{19}H_{12}O_4$ requires C, 75·0; H, 3·95; OMe, 10·2%). The benzene mother-liquors from the reaction mixture were concentrated, to give a second crop (*ca.* 1·55 g.), m. p. 205—210°. On crystallisation of this from benzene, the first fraction proved to be the above anhydride (Im). The second fraction, m. p. 220—250° (*ca.* 1·8 g.), gave, on repeated crystallisation from the same solvent, the *anhydride* (II) in pale yellow crystals, m. p. 266—268°, depressed on admixture with its above isomer, with 7-methoxy-1-*p*-methoxyphenyl-,[5] and with 1-phenyl-naphthalene-2 : 3-dicarboxylic anhydride (Found: C, 74·9; H, 3·9%).

1-p-*Methoxyphenylnaphthalene* (IVm).—1-*p*-Methoxyphenylnaphthalene-2 : 3-dicarboxylic acid (0·5 g.) (prepared from the anhydride) was decarboxylated with copper-bronze (0·4 g.) in quinoline (5 ml.) as usual. The product was distilled (b. p. 176—178°/1 mm.), then crystallised from dilute ethanol, to give 1-*p*-methoxyphenylnaphthalene (*ca.* 0·3 g.), m. p. 116—116·5°, undepressed on admixture with an authentic specimen [14] (Found: C, 87·0; H, 5·8; OMe, 12·8. Calc. for $C_{9}H_{14}O$: C, 87·2; H, 6·0; OMe, 13·0%).

A'IN-SHAMS UNIVERSITY, CAIRO, EGYPT. [*Received, August* 22*nd*, 1958].

[11] Skraup and Schwamberger, *Annalen*, 1928, **462**, 148.
[12] von Braun, *Annalen*, 1927, **451**, 44.
[13] Schroeter, *Ber.*, 1930, **63**, 1308.
[14] Howell and Robertson, *J.*, 1936, 587.

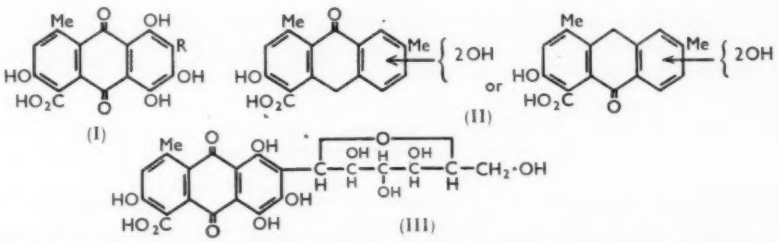
210. *C-Glycosyl Compounds. Part III.* Carminic Acid.*

By M. A. Ali and L. J. Haynes.

Carminic acid is shown to be the *C*-glucopyranosyl compound (III) by ozonolysis to give arabinose and by periodate oxidation of methyl carminate tetramethyl ether.

Carminic acid was given the structure (I; R = $C_6H_{11}O_5$) by Dimroth and Kamerer.[1] This paper is concerned with the structure of the side chain R.

Earlier workers [1,2] had shown by acetylation that this side chain contains four hydroxyl groups. In 1926, Miyagawa [3] showed that ozonolysis of carminic acid in water gave oxalic acid and a small quantity of a colourless optically active product. The latter with barium permanganate gave an amorphous optically active acid, probably $C_6H_{12}O_6$, which was reduced by sodium amalgam to a sugar ($C_6H_{12}O_5$) which was not identical with any known methylpentose. By analogy with the structure proposed for kermesic acid (I; R = Ac), Miyagawa suggested structure {I; R = CO·[CH(OH)]$_4$·CH$_3$} for carminic acid, but this was criticised by Todd [4] as being difficult to reconcile with the formation of coccinin (II) when carminic acid is fused with alkali. It was more likely that carminic acid was a *C*-glycosyl compound.[5]



Carminic acid with diazomethane gave methyl carminate tetramethyl ether (methylation of the four phenolic hydroxyl groups), which at 0° consumed 2·1 mol. of periodate with the formation of formic acid. This showed the presence of a C(OH)·CH(OH)·C(OH) system in the side chain and that Miyagawa's structure, which would require consumption of at least 3 mols. of oxidant, is incorrect.

Now we had shown [6] that oxidation of barbaloin with ferric chloride gave D-arabinose in good yield; further examination of this revealed that a second sugar is also formed, in much smaller amount, which gives a yellow colour with aniline oxalate and is identical on paper chromatography with glucose (see Table). We have not been able to identify this material rigidly by conversion into a crystalline derivative, probably because the amounts formed in the oxidation are so small, but there can be little doubt that it is D-glucose especially since barbaloin is known to be a glucose derivative. Similar oxidation of carminic acid gave a solution which on paper chromatography appeared to contain very small quantities of the same two sugars. Ozonolysis of carminic acid gave the same two sugars in rather better yield. They were separated by chromatography on thick paper

* The papers in *J.*, 1956, 3141, and *J.*, 1958, 2231, are regarded as Parts I and II of this series.

[1] Dimroth and Kamerer, *Ber.*, 1920, **53**, 471. For reviews of the work of Liebermann, von Miller, and Dimroth and their co-workers leading to this structure see Pollard and Cross in Thorpe's "Dictionary of Applied Chemistry," 4th edn., 1939, Vol. III, p. 226, and Thomson, "Naturally Occurring Quinones," Butterworths, London, 1957, pp. 222—227.

[2] von Miller and Rohde, *Ber.*, 1897, **30**, 1759.

[3] Miyagawa, *Mem. Coll. Eng. Kyushu Imp. Univ.* (*Japan*), 1924, **4**, 99; *Chem. Abs.*, 1927, **21**, 1127.

[4] Todd, *Ann. Reports*, 1941, **38**, 214.

[5] See, *e.g.*, Fieser and Fieser, "Textbook of Organic Chemistry," Heath, Boston, 1944, 857.

[6] Hay and Haynes, *J.*, 1956, 3141.

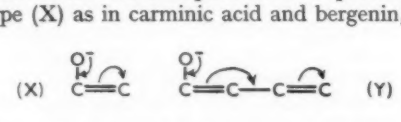
and one was rigidly identified as arabinose, but an attempt to confirm the identification of the other as its *p*-nitroaniline derivative was unsuccessful. Paper chromatography showed that the same two sugars were also formed on ozonolysis of barbaloin.

These results show that the side chain in carminic acid is glucopyranosyl. Unfortunately, from our degradation experiments we had insufficient arabinose to be able to determine its rotation, but since, following a suggestion of the Referees, we have found that L-arabinose benzoylhydrazone depresses the m. p. of the D-compound, the arabinose must be D-arabinose and there can be little doubt that carminic acid is the D-glucopyranosyl derivative (III).

Sugar	R_{xylose} in *A*	R_{xylose} in *B*	Colour with aniline oxalate
Arabinose	0·80; 0·82	0·82	Pink
Glucose	0·71; 0·69	0·50	Yellow
Sugars from barbaloin by $FeCl_3$	0·80	0·82	Pink
	0·68	0·52	Yellow
Sugars from carminic acid by $FeCl_3$	0·79; 0·82	0·83	Pink
	0·66; 0·69	0·54	Yellow
Sugars from barbaloin by O_2	0·82	—	Pink
	0·70	—	Yellow
Sugars from carminic acid by O_2	0·81	—	Pink
	0·69	—	Yellow

A = Butan-1-ol–pyridine–water (10 : 3 : 3). *B* = Butan-1-ol–acetic acid–water (2 : 1 : 1).

For formation of these *C*-glycosyl compounds in Nature it may be assumed that the "aglycone" is formed first: removal or separation of a proton from the aglycone then gives a system of the type (X) as in carminic acid and bergenin,[7] or (Y) as in barbaloin,



(X) (Y)

so that the glycosyl residue may be introduced on oxygen to give a glycoside or on carbon to give a *C*-glycosyl compound. In unpublished work we have shown that resorcinol readily forms a *C*-glycopyranosyl derivative and it seems likely that there exist in Nature *C*-glycosyl isomers of many of the glycosides of 1 : 3-dihydric phenols.

Experimental

Carminic acid (12·1 g.), isolated [8] from dried *Dactylopius coccus* Costa (250 g., "silver grain"), darkened at 120° and had R_F 0·17 in propan-1-ol–ammonia (*d* 0·880)–water (6 : 3 : 1) and 0·12 in butan-1-ol–pyridine–water (3 : 1 : 1), and $\nu_{max.}$ in Nujol 1708s, 1693s, 1677m, 1648m, 1632m, 1606s, 1566s, 1509 cm.$^{-1}$. With N-sulphuric acid at 100° for 4 hr. or with emulsin in acetate buffer pH 5 for 4 days it gave no sugar (paper chromatography). In periodate oxidation for 4 hr. at 0° there was a consumption of 6·2 mol.

Methyl Tetra-O-methylcarminate.—Carminic acid (2 g.) in anhydrous methanol (150 ml.) was cooled to 5° and diazomethane (*ca.* 2·5 g.) in dry ether (100 ml.) slowly added. There was a vigorous evolution of nitrogen and some carminic acid was precipitated. The mixture was kept at room temperature. After 16 hr. the solution was pale brown-red and most of the precipitated acid had redissolved. The mixture was warmed (60—65°) to remove excess of diazomethane and ether, cooled, filtered, and evaporated under reduced pressure (nitrogen). The residual, dark brown-red oil was chromatographed on magnesium carbonate (12 × 2·1 cm.), benzene being used as solvent and eluant; carminic acid and other impurities remained as a top, broad red band. The product separated as a brown-yellow band which on elution gave a deep yellow solution which was concentrated to *ca.* 10 ml. and rechromatographed. The bright yellow eluate was concentrated to a solution which was brownish-red by reflected and yellow by transmitted light. Removal of solvent under reduced pressure (nitrogen) gave a yellow glass. Slow evaporation (2 weeks) of a solution of this glass in benzene–light petroleum (b. p. 40—60°)

[7] Hay and Haynes, *J.*, 1958, 2231.
[8] Schunk and Marchlewski, *Ber.*, 1894, **27**, 2979; Dimroth and Scheurer, *Annalen*, 1913, **399**, 43.

gave *methyl tetra*-O-*methylcarminate* as yellow needles m. p. 185—188° [Found: C, 57·0; H, 5·4; OMe, 27·8, 28·1. $C_{22}H_{15}O_8(OMe)_8$ requires C, 57·6; H, 5·3; OMe, 27·6%].

Periodate Oxidation.—An aqueous solution of the methylation product (25·1 mg.) and 0·5M-sodium metaperiodate (10 ml.) were mixed, the whole was made up to 20 ml. with distilled water, and the solution set aside at 0°. The oxidation was followed by the titration of aliquot parts (2 ml.): it was complete in 2 hr., 2·1 mol. of oxidant being consumed and the solution becoming turbid. In another experiment, the solution was steam-distilled when the oxidation was complete, and formic acid was detected in the steam-distillate by Feigl's method.[9]

Ozonolysis of Carminic Acid.—2% Ozonised oxygen was passed through a cooled solution of carminic acid (3 g.) in water (60 ml.) until the colour changed from red to brownish-yellow (*ca.* 3 hr.). The solution was then steam-distilled: the distillate gave a positive test for formaldehyde with chromotropic acid. The aqueous residue, which became dark brown during the distillation, was extracted with ether (3 × 200 ml.), and the aqueous phase evaporated to dryness under reduced pressure. The residue, a dark brown syrup, was redissolved in water (200 ml.), and saturated aqueous lead acetate was added: a yellow-grey solid which was precipitated was removed. Excess of lead was removed from the filtrate by two treatments with hydrogen sulphide. The final aqueous solution was evaporated to dryness, giving pale yellow syrup (310 mg.); paper chromatography showed the presence of two sugars (see Table).

D-*Arabinose Benzoylhydrazone.*—The above syrup was chromatographed on several pieces of Whatman 3 mm. paper which had previously been continuously extracted with benzene–ethanol. The appropriate sections of the papers were eluted with water to give the two sugars as pale yellow syrups. On treatment with benzoylhydrazine in ethanol the syrup believed to be arabinose gave D-arabinose benzoylhydrazone, m. p. 184—187° (decomp.), undepressed on admixture with the authentic hydrazone,[10] m. p. 184—188° (decomp.).

We thank the Government of Pakistan for a scholarship and the Distillers Company Limited for a grant (to M. A. A.), T. and H. Smith Limited, Edinburgh, for gifts of *D. coccus*, and Dr. J. Evelyn Hay for advice and assistance.

UNIVERSITY COLLEGE OF THE WEST INDIES,
KINGSTON 7, JAMAICA. [*Received, October 9th,* 1958.]

[9] Feigl, "Spot Tests," English translation by R. E. Oesper, Elsevier, Amsterdam, 1954, p. 246.
[10] Hirst, Jones, and Woods, *J.*, 1947, 1048.

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211. *Kinetics of the* N-*Alkylation of Diarylamines by Methyl Iodide in* NN-*Dimethylformamide.*

By SAUL PATAI and SHMUEL WEISS.

The reaction of alkyl halides with diphenylamine in different solvents has been studied. The kinetics of the reaction of methyl iodide with diphenylamine and di-*p*-tolylamine has been measured in *NN*-dimethylformamide. This reaction takes place by a bimolecular substitution mechanism between the two un-ionised reactant molecules.

THE *N*-alkylation of diarylamine derivatives is generally carried out under drastic conditions,[1] so no proper kinetic investigation is feasible. We have carried out the alkylation so that the kinetics should be measurable, and thence deduced the mechanism of the reaction. Both the alkyl halides and the solvents led to experimental difficulties. With benzyl chloride the reaction could be carried out readily in ethanol, but side reactions constituted 25% of the total reaction of the halide. With benzyl chloride in benzyl alcohol, in kinetic experiments, the concentration of the free acid started to *fall* after a certain time. Benzyl alcohol and dry hydrogen chloride react with each other, forming (probably) benzyl chloride.[2] In inert solvents, such as benzene, nitrobenzene, dioxan, ethyl acetate, and acetone, diphenylamine and benzyl chloride did not react at 60° in

[1] Wedekind, *Ber.*, 1899, **32**, 511.
[2] Cannizzaro, *Annalen*, 1853, **88**, 130; Norris, *Amer. Chem. J.*, 1907, **38**, 631.

18—20 hr., and only reacted very slowly (about 1—2% in 18 hr.) in nitromethane, acetonitrile, dimethylformamide, or an excess of benzyl chloride.

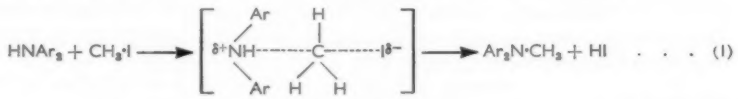
TABLE 1. *Second-order rate coefficients of the reaction of diphenylamine and of di-*p*-tolylamine with methyl iodide in dimethylformamide at* 40°.

Diphenylamine (mole l.$^{-1}$) ...	0·25	0·5	0·5	1·0	1·0	1·0			
Methyl iodide (mole l.$^{-1}$)	1·0	0·5	1·0	0·25	0·5	1·0			
10^6k_2 (l. mole^{-1} sec.$^{-1}$)	3·72	3·80	3·65	3·72	3·76	3·61			
	3·80		3·72	3·80	3·72	3·62			
Di-*p*-tolylamine (mole l.$^{-1}$) ...	0·25	0·25	0·25	0·5	0·5	0·5	1·0	1·0	1·0
Methyl iodide (mole l.$^{-1}$)	0·25	0·5	1·0	0·25	0·5	1·0	0·25	0·5	1·0
10^6k_2 (l. mole^{-1} sec.$^{-1}$)	18·8	18·3	17·4	18·3	18·4	17·7	18·1	17·6	17·3

It seemed that in solvents of low dielectric constant the reaction did not take place; a higher dielectric constant was a necessary but not a sufficient condition. On the other hand, protogenic solvents of intermediate dielectric constants such as alcohols, etc., while giving conveniently measurable rates, gave also side reactions at a comparatively high rate. It was decided, therefore, to use dimethylformamide as solvent, as it has an intermediate dielectric constant ($\varepsilon = 37{\cdot}6$ at 20°). Although this solvent has no active hydrogen atom comparable to that in hydroxylic solvents, yet in certain circumstances [3] it may give protons, and so can probably form hydrogen bonds, which seem to be necessary for the alkylation to take place under mild conditions.

In view of these considerations, the choice was narrowed to the reaction of diarylamines with methyl iodide in dimethylformamide at 40°. The results for diphenylamine and di-*p*-tolylamine are shown in Table 1; with di-(*p*-nitrophenyl)amine and dipicrylamine the reaction was too slow to be followed. Reproducibility is good; the second-order rate coefficients are almost constant at the concentrations investigated.

The reaction takes place probably through a bimolecular (S_N2) mechanism:



. . . (I)

In this, the rate-determining step is the formation of the intermediate, and it is reasonable to suppose that both reactants start in their molecular, uncharged form. The following argument can be put forward to support this scheme: The large effect of the polarity of the various solvents fits either a bimolecular mechanism between two *uncharged* molecules, or a unimolecular one with the ionisation of the alkyl halide as the rate-controlling step.[4] The second possibility is eliminated by the strictly second-order kinetic form. Another possible mechanism would involve reaction of a pre-formed diarylamine anion (Ar_2N^-) with a neutral alkyl halide molecule in the rate-determining step; this should give second-order kinetics, but would be influenced adversely by the polarity of the solvent, being between one charged and one neutral entity.[4] Still, the polarity might enhance the rate by displacing the equilibrium $Ar_2NH \rightleftharpoons Ar_2N^- + H^+$ strongly towards the right; the reaction would then be faster because of the influence of polarity on the *amount* of one of the reacting species, *i.e.*, the diarylamine anion. However, since the acidity of diarylamines is strongly enhanced by electron-withdrawing substituents such as nitro-groups, and diminished by electron-repelling substituents such as methyl groups, then if the magnitude of the ionisation of the diarylamine influences the rate of the reaction, di-*p*-tolylamine should react more slowly than diphenylamine, and di-*p*-nitrophenylamine much faster. In fact the opposite is true. Hence we prefer the mechanism (I).

[3] Given, *J.*, 1958, 2686; Wawzonek, Blaha, Berkey, and Runner, *J. Electrochem. Soc.*, 1955, **102**, 235.

[4] Ingold, " Structure and Mechanism in Organic Chemistry," G. Bell and Sons Ltd., London, 1953, p. 347.

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Experimental

Materials.—All solvents were redistilled pure commercial products. Diphenylamine (B.D.H.), recrystallised several times from ethanol until colourless, had m. p. 53—54°. Di-*p*-tolylamine (m. p. 79°) was prepared according to Girard *et al.*[5] Di-(*p*-nitrophenyl)amine (m. p. 218—221°) was prepared according to Gnehm and Werdenberg.[6]

Table 2. *Reaction of various alkyl halides* (1M) *with diphenylamine* (1M) *in different solvents and with the solvents alone.*

			Reaction with $NHPh_2$ and solvent		Reaction with solvent alone	
RX	Solvent	Temp.	Reaction time (hr.)	% Reaction of RX *	Reaction time (hr.)	% Reaction of RX *
CH_2PhCl	Abs. EtOH	60°	16	20	16	5
,,	$CH_2Ph{\cdot}OH$	60	16	23	16	2
,,	,,	40	24	7	24	0
,,	$H{\cdot}CO{\cdot}NMe_2$	60	15	1	15	0
EtBr	Abs. EtOH	60	48	32	17	3
Bu^nBr	,,	60	48	10	16	1
,,	$H{\cdot}CO{\cdot}NMe_2$	60	15	1	—	—
Pr^iBr	Abs. EtOH	60	48	20	28	2
Bu^tCl	$H{\cdot}CO{\cdot}NMe_2$	60	18	2	—	—
MeI	,,	40	17	24	17	1

* Amount of HX formed, determined by titration.

Reaction Measurements (*see Table* 2).—The reactions were carried out in an oil-bath whose temperature was constant within ±0·05°. The percentage of reaction after 16—48 hr. was determined by titration of 1 or 2 ml. samples, diluted with ethanol, with ethanolic potassium hydroxide, Bromocresol Green being the indicator. The appearance of the final blue (basic) colour was usually taken as the end-point, but if the reaction mixture was yellow or light red it was easier to titrate to the green (intermediate) colour of the indicator.

Controls. Benzyl alcohol reacted with dry hydrogen chloride at 40—60°: the reaction was carried out in closed ampoules, so acid could not evaporate. Hydrogen chloride also reacted with dimethylformamide slowly at 40° and rapidly at 100°. In these reactions the products were not identified but loss of acid was determined by titration. No measurable reaction took place between hydriodic acid and dimethylformamide at 40° during 17 hr.

Rate measurements. The appropriate amount of diarylamine was weighed in a 25 ml. measuring flask and dissolved in about 20 ml. of dimethylformamide. When this had reached the reaction temperature methyl iodide was added from an accurate pipette, and the flask was immediately filled to the mark with dimethylformamide at 40°, and shaken thoroughly. Samples of 2 ml. were taken with pipettes (also kept at 40°). The first sample was taken within 1 min. of mixing, and subsequent samples at intervals of about 30 min. The samples were diluted with 3 ml. of ethanol [for di-(*p*-nitrophenyl)amine with 5 ml. of acetone, to avoid precipitation] and titrated with 0·01N-ethanolic potassium hydroxide (Bromocresol Green indicator). A " blank " was conducted, whose results indicated the reaction of methyl iodide with solvent. As shown in Table 3, this reaction was comparatively slow, and was assumed to run concurrently with, but independently of, the main reaction. The " blank " values were subtracted from the measured values. The nature of this " blank " reaction was not clarified, but even in 5—6 hr. it used less than 0·5% of the methyl iodide present.

Calculation of Rate Coefficients.—Rate coefficients were calculated from the integrated form of the second-order rate expression $dx/dt = k_2(a - x)(b - x)$. In most cases the measured values (*i.e.*, the corrected volumes of KOH used *versus* time) fell on a straight line, showing that the " initial rate " expression may be used for calculation. In those cases, since $dx/dt = k_2ab$ (a and b being the initial concentration of methyl iodide and of the diarylamine respectively), k_2 could be calculated directly from the slope. The two methods gave good agreement (see note to Table 3).

[5] Girard, De Laire, and Chapoteaut, *Annalen*, 1866, **140**, 346.
[6] Gnehm and Werdenberg, *Z. angew. Chem.*, 1899, **12**, 1051.

Analysis of Products.—Methyl iodide (1M) and diphenylamine (0·5M) were heated together at 40° for 3 days. The amount of hydrogen chloride then found by titration corresponded to 70% reaction of the amine. The solvent and excess of methyl iodide were evaporated *in vacuo*. Water and chloroform were added to the residue and the chloroform solution was evaporated. Concentrated hydrochloric acid was added to the residue, and precipitated diphenylamine

TABLE 3. *Reaction of diphenylamine* (0·5M) *with methyl iodide* (0·5M) *in dimethylformamide at* 40°.

Time (min.)	0·0093N-KOH (ml.) used	for blank	corr.	$NHPh_2$ reacted (%)	10^6k_2 * (l. sec.$^{-1}$ mole^{-1})	Time (min.)	0·0093N-KOH (ml.) used	for blank	corr.	$NHPh_2$ reacted (%)	10^6k_2 * mole^{-1}) mole^{-1})
1	0·05	0·05	0·00	0·00	—	150	2·15	0·30	1·85	1·72	3·83
30	0·45	0·10	0·35	0·32	3·62	180	2·55	0·35	2·20	2·05	3·79
60	0·85	0·20	0·65	0·60	3·36	210	3·00	0·40	2·60	2·42	3·84
90	1·30	0·25	1·05	0·98	3·62	270	3·85	0·50	3·35	3·12	3·85
120	1·75	0·25	1·50	1·40	3·88	330	4·60	0·50	4·10	3·82	3·85

* Mean of all values in this column: $3·74 \times 10^{-6}$ l. sec.$^{-1}$ mole^{-1}; k_2 determined from graph of ml. of KOH (corr.) *versus* time: $3·80 \times 10^{-6}$ l. sec.$^{-1}$ mole^{-1}.

hydrochloride filtered off. Sodium hydroxide was added to the filtrate until basic, and the *N*-methyldiphenylamine extracted with ether. Evaporation of the ether yielded 1·7 g. of an oil, n_D^{20} 1·615 (Brühl [7] gives 1·6107 for *N*-methyldiphenylamine).

The reaction of di-*p*-tolylamine (0·5M) and methyl iodide (1·0M) was complete after 3 days. After evaporation of the solvent *in vacuo*, the residue was washed with dilute aqueous potassium hydroxide (5%) and taken up with ether. After evaporation, an oil was obtained (85% yield) which solidified on standing (m. p. 33° undepressed on admixture with an authentic sample [8] of the *N*-methyl derivative).

Green by-product. In all experiments with diphenylamine and benzyl chloride the reaction mixture was deep emerald-green. A similar colour developed more slowly in all experiments where diphenylamine reacted with alkyl halides in benzyl alcohol and also when diphenylamine was heated with a solution of hydrogen chloride in benzyl alcohol. No colour developed if no reaction took place between the amine and the alkyl halide, *e.g.*, with *n*-butyl chloride. The intensity of the green colour seemed to depend on the amount of air in contact with the mixture: mixtures degassed and filled into ampoules *in vacuo* developed only a very faint green tinge.

A few mg. of the impure green dye were prepared as follows: diphenylamine (1 mole) was refluxed with benzyl chloride (1 mole) in ethanol (1 l.) for 10 hr. After cooling, the mixture was filtered from the benzyldiphenylamine (73 g.), and water added to the filtrate. The lower, dark green layer, consisting mainly of benzyl chloride, was separated and a large excess of dry ether was added to it; a dark green precipitate was formed (~34 mg.) which was soluble in ethanol and in acetic acid and insoluble in ether and in water. Its ethanolic solution was green in acid and red in basic media. The ultraviolet-light absorption of the green form in ethanol showed a broad maximum at 450—475 mμ and a sharp peak at 640 mμ. For comparison, a green substance was prepared from diphenylamine by oxidation with ferric chloride,[9] but it had absorption maxima at 430 and at 750 mμ. Our substance could not be purified and was not further investigated.

DEPARTMENT OF ORGANIC CHEMISTRY,
THE HEBREW UNIVERSITY, JERUSALEM, ISRAEL. [*Received, October 15th*, 1958.]

[7] Brühl, *Annalen*, 1886, **235**, 21.
[8] Girard, *Bull. Soc. chim. France*, 1875, **24**, 120.
[9] Vogel, "Quantitative Inorganic Analysis," 2nd Edn., Longmans, Green & Co., London, 1951, p. 91.

XUM

212. *The Heterogeneous Polymerization of α-N-Carboxyamino-acid Anhydrides.*

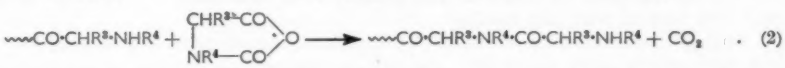
By D. G. H. Ballard and C. H. Bamford.

The polymerizations of the *N*-carboxy-anhydrides of sarcosine, L-alanine, L-leucine, and L-proline initiated by primary bases have been studied in conditions such that polymers are precipitated at an early stage of reaction. In each case separation of polymer is accompanied by an increase in rate. It is concluded that the increase arises primarily from the heterogeneity, and possible mechanisms are discussed. The bearing of these results on the postulated existence of two successive propagation coefficients in the polymerization of the *N*-carboxy-anhydrides of optically active α-amino-acids is considered.

The mechanism of polymerization of the *N*-carboxy-anhydrides of DL-α-amino-acids in solution has been the subject of numerous investigations. When primary or secondary bases are used as initiators the base adds to $C_{(5)}$, and subsequent ring opening and elimination of carbon dioxide lead to formation of a substituted amide of the amino-acid:[1,2]

$$NHR^1R^2 + \begin{matrix} CHR^3{-}CO \\ | \quad\quad O \\ NR^4{-}CO \end{matrix} \longrightarrow NR^1R^2{\cdot}CO{\cdot}CHR^3{\cdot}NHR^4 + CO_2 \quad . \quad . \quad . \quad . \quad . \quad (1)$$

This product, being a base, can react similarly with further molecules of anhydride to form a linear polypeptide. The general propagation reaction is shown in (2):



$$\sim\!\!\sim CO{\cdot}CHR^3{\cdot}NHR^4 + \begin{matrix} CHR^3{-}CO \\ | \quad\quad O \\ NR^4{-}CO \end{matrix} \longrightarrow \sim\!\!\sim CO{\cdot}CHR^3{\cdot}NR^4{\cdot}CO{\cdot}CHR^3{\cdot}NHR^4 + CO_2 \quad . \quad (2)$$

Kinetic investigations have indicated that if $R^4 = H$ this reaction is of first order in anhydride and base concentrations. In the general case the velocity coefficients of initiation and of propagation are different, but all the propagation steps, with the exception of the first two, probably have similar coefficients.[1] A particularly simple situation arises when initiation is carried out by a preformed short polymer; the overall reaction is then of first order throughout its whole course. With *N*-carboxysarcosine anhydride ($R^3 = H$, $R^4 = Me$) the propagation reaction is complicated by catalysis by carbon dioxide,[1] probably through the participation of carbamate ions.

Some *N*-carboxy-anhydrides, particularly those derived from optically active amino-acids, cannot be polymerized in homogeneous systems on account of the insolubility of the resulting polypeptides in suitable reaction media. When studying one such polymerization—that of α-*N*-carboxy-L-alanine anhydride in nitrobenzene—we found that a marked acceleration occurs when the system becomes heterogeneous. About this time Doty and Lundberg [3] and Lundberg and Doty [4] published results on the polymerization of the γ-benzyl ester of α-*N*-carboxy-L-glutamic anhydride in dioxan solution which were interpreted in terms of two successive propagation coefficients; the first corresponded to the growth of the chains up to a certain critical size, and the second, about five times as large, was considered to apply to subsequent growth. Similar observations were later reported by Idelson and Blount [5] and Weingarten.[6] Lundberg and Doty, on the basis of optical-rotation studies by Mitchell, Woodward, and Doty,[7] suggested that chains shorter than the critical size were predominantly randomly coiled, while those larger were mainly

[1] Ballard and Bamford, *Proc. Roy. Soc.*, 1954, *A*, **223**, 495.
[2] Breintenbach and Allinger, *Monatsh.*, 1953, **84**, 1103.
[3] Doty and Lundberg, *J. Amer. Chem. Soc.*, 1956, **78**, 4810.
[4] Lundberg and Doty, *ibid.*, 1957, **79**, 3961.
[5] Idelson and Blout, *ibid.*, p. 3948.
[6] Weingarten, *ibid.*, 1958, **80**, 352.
[7] Mitchell, Woodward, and Doty, *ibid.*, 1957, **79**, 3955.

α-helical; the latter configuration was therefore supposed to give rise to an increased rate of propagation. This idea has been elaborated by Weingarten,[6] who has considered in detail the nature of the transition state in the mechanism of propagation involving α-helical polypeptides. We have not been able to confirm these findings with the γ-benzyl ester of α-*N*-carboxy-L-glutamic anhydride.[8] The anhydride is not ideal for kinetic work because it cannot be purified by sublimation and some of the recorded differences may be due to the presence of traces of unidentified impurities.

Lundberg and Doty [4] recently extended their work to include the polymerization of α-*N*-carboxy-L-leucine anhydride in nitrobenzene and reported essentially similar results to those they obtained with the γ-benzyl ester of α-*N*-carboxy-L-glutamic anhydride. They mentioned that the system is heterogeneous but did not consider that this feature affected their interpretation in terms of configurational changes of the growing chains. It appeared to us that this polymerization is similar to that of α-*N*-carboxy-L-alanine anhydride in nitrobenzene already mentioned and we have undertaken a kinetic investigation of these and other heterogeneous polymerizations. This work is reported in the present paper. All four systems studied show similar kinetic features which we attribute to the onset of heterogeneity.

Experimental

Materials.—The *N*-carboxy-anhydrides of sarcosine, L-alanine, L-leucine, and L-proline, prepared by standard methods,[9,10] were recrystallized from the solvents mentioned in the literature until completely free from chlorine (<0·01 mole %) and were sublimed in a vacuum before use.

The purification of nitrobenzene has already been described.[1] " AnalaR " benzene was stored over sodium wire and distilled.

" AnalaR " *n*-hexylamine was dried (KOH pellets), then distilled in a vacuum into ampoules which were subsequently sealed off. The preparation and purification of sarcosine dimethylamide were carried out as described earlier.[1]

Apparatus and Technique.—The rates of polymerization of the *N*-carboxy-anhydrides were generally measured by the rates of evolution of carbon dioxide in a constant-volume apparatus,[1] but a few experiments were carried out in a constant-pressure apparatus [1] or under conditions of virtually zero carbon dioxide pressure.[11] The last experiments were necessary to establish that catalysis of the reactions by carbon dioxide [1] did not play a significant part in the constant-volume experiments.

Access of atmospheric moisture to the reactants was excluded by conducting all manipulations involved in preparing the reaction vessel in a dry box.[1]

In all the experiments described below, the *N*-carboxy-anhydrides were initially completely dissolved in the reaction media.

Results and Discussion

(i) *The* α-N-*Carboxysarcosine Anhydride–Benzene System.*—The results of initiation by *n*-hexylamine are shown in Figs. 1, 2(*a*), and 2(*b*) for three different base concentrations, $[M]/[M]_0$ being plotted logarithmically as a function of time. Here [M] is the anhydride concentration at time *t*. Each curve consists of four portions. The initial steep portion *AB* corresponds to the reaction of *n*-hexylamine with the anhydride; this base is stronger than the basic derivative subsequently produced and hence reacts faster. This type of behaviour has already been referred to and has no special interest here. From *B* to *C*, $\log [M]/[M]_0$ is approximately linear in *t*; at *C* the slope of the plot begins to increase but eventually a second nearly linear portion is observed, extending to *D*. After *D* the slope begins to decrease progressively. A comparison of Figs. 1, 2(*a*), and 2(*b*) shows that the relative importance of the various steps depends on the initiator concentration.

[8] Ballard and Bamford, *J. Amer. Chem. Soc* 1957 **79**, 2336.
[9] Hanby, Waley, and Watson, *J.*, 1950, 3009.
[10] Katchalsky, Kurtz, Fasman, and Berger, *Bull. Res. Council Israel*, 1956, **5**, *A*, No. 4.
[11] Ballard, Bamford, and Weymouth, *Proc. Roy. Soc.*, 1955, *A*, **227**, 155.

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As far as can be ascertained visually, the system becomes heterogeneous just before the point *C* is reached in each case. Between *C* and *D* the polymer is dispersed, while after *D* coagulation to a more compact precipitate occurs.

The calculated number average degrees of polymerization corresponding to the points *C* and *D* are given in the Table, together with the approximate velocity coefficients, $-(d[M]/dt)/[M][X]$, for the steps *BC*, *CD*. Here [X] represents the (constant) base concentration. A run was carried out with sarcosine dimethylamide as initiator in place of *n*-hexylamine, having [M]/[X] = 10 initially. The results were indistinguishable from those with *n*-hexylamine.

FIG. 1. *Reaction of* N-*carboxysarcosine anhydride with* n-*hexylamine in benzene at* 25°: $[M]_0 = 0{\cdot}100$ mole l.$^{-1}$; $[X]_0 = 10^{-2}$ mole l.$^{-1}$.

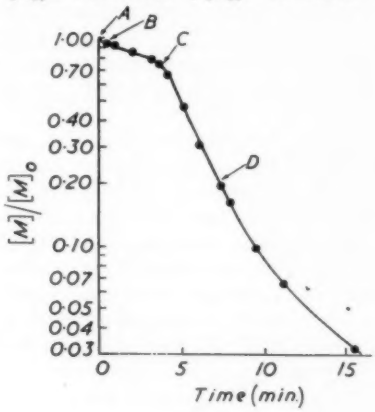
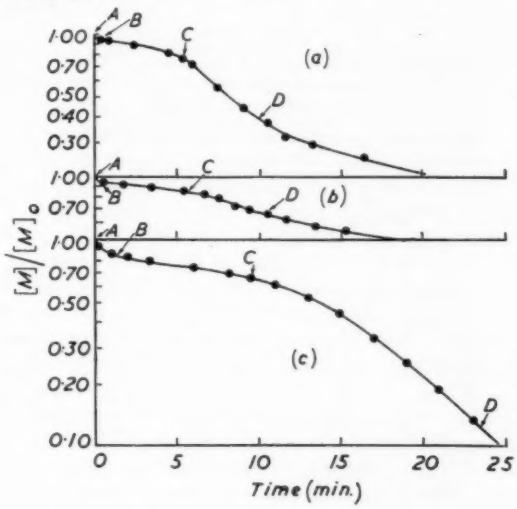


FIG. 2. (*a*), (*b*) *Reaction of* N-*carboxysarcosine anhydride with* n-*hexylamine in benzene at* 25°: $[M]_0 = 0{\cdot}100$ mole l.$^{-1}$; $[X]_0 = (a)\ 5{\cdot}3 \times 10^{-3}$, (*b*) $2{\cdot}6 \times 10^{-3}$ mole l.$^{-1}$. (*c*) *Reaction of* N-*carboxy-*L-*alanine anhydride with* n-*hexylamine in nitrobenzene at* 25°: $[M]_0 = 0{\cdot}102$ mole l.$^{-1}$; $[X]_0 = 10^{-2}$ mole l.$^{-1}$.



[M]/[X] (initial)	Approx. velocity coeff. (mole^{-1} l. min.$^{-1}$) *B–C*	*C–D*	Number average degree of polymerization *C*	*D*
10·0	6·6	38	3	8
18·9	7·8	34	4	12
38·4	7·1	39	6	12

The increase in rate at the point *C* corresponds to a factor of 5 or 6, while the number average degree of polymerization is in the range 3—6. It is most unlikely that polysarcosine undergoes any definite configurational change in this range. In particular, since polysarcosine is an *N*-substituted polypeptide it cannot adopt an α-helical configuration, hence explanations of the rate data based on special steric features of this configuration [6] do not apply.

The rate of the polymerization reaction (2) in nitrobenzene solution at zero carbon dioxide pressure is of strictly first order in base and anhydride concentrations throughout,[12] so it is unlikely that any chemical factor is responsible for the effects observed in the present case.

(ii) *Systems containing* α-N-*Carboxy-*L-*alanine Anhydride.*—A typical run with this anhydride in nitrobenzene is shown in Fig. 2(*c*). The curve is essentially similar to that

[12] Ballard and Bamford, to be published.

in Fig. 1 for α-*N*-carboxysarcosine anhydride in benzene. The rate of polymerization increases markedly—by a factor of about 5·5—when the number average degree of polymerization reaches 4 (in the neighbourhood of *C*) and the reaction eventually follows a course in which log [M] is approximately linear in *t*. In this case gelation occurs just before the increase in rate sets in.

Similar polymerizations carried out in benzene are represented in Figs. 3(*a*) and (4*a*). Fig. 3(*a*) is similar to Fig. 2(*c*); the rate increases by a factor of 8·5 when the number average reaches 3 (near *C*). Fig. 4(*a*), which refers to a higher initial value of [M]/[X], shows four portions similar to those observed in the experiments with α-*N*-carboxysarcosine anhydride (Fig. 1). Here the rate increases by a factor of 14·5 when the number average degree of polymerization attains a value of 5 (near *C*). As is the case with the sarcosine

FIG. 3. (*a*) *Reaction of* N-*carboxy*-D-*alanine anhydride with* n-*hexylamine in benzene at* 25°: $[M]_0 = 0{\cdot}113$ mole l.$^{-1}$; $[X]_0 = 10^{-3}$ mole l.$^{-1}$. (*b*) *Reaction of* N-*carboxy*-L-*proline anhydride with* n-*hexylamine in nitrobenzene at* 25°: $[M]_0 = 9{\cdot}8 \times 10^{-2}$ mole l.$^{-1}$; $[X]_0 = 10^{-2}$ mole l.$^{-1}$.

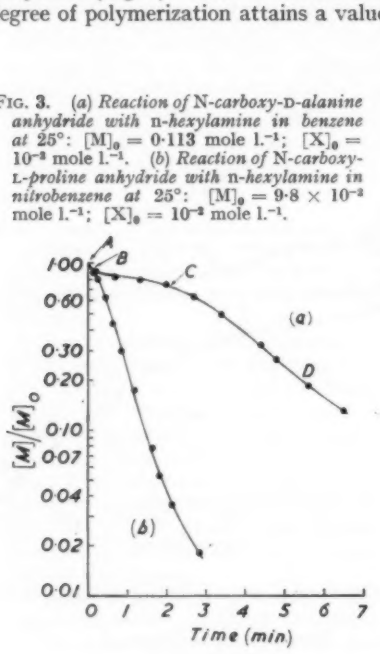
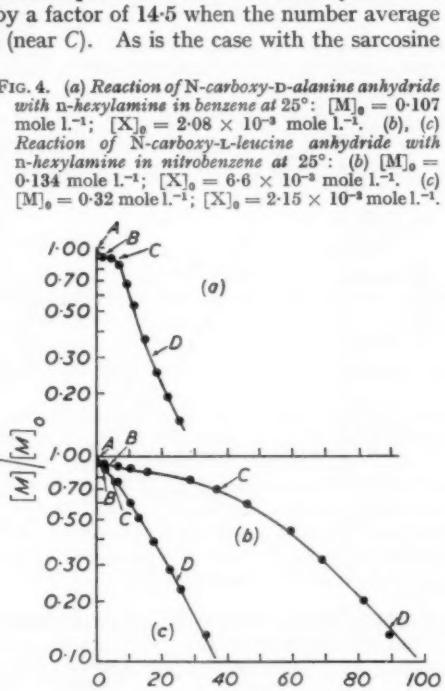


FIG. 4. (*a*) *Reaction of* N-*carboxy*-D-*alanine anhydride with* n-*hexylamine in benzene at* 25°: $[M]_0 = 0{\cdot}107$ mole l.$^{-1}$; $[X]_0 = 2{\cdot}08 \times 10^{-3}$ mole l.$^{-1}$. (*b*), (*c*) *Reaction of* N-*carboxy*-L-*leucine anhydride with* n-*hexylamine in nitrobenzene at* 25°: (*b*) $[M]_0 = 0{\cdot}134$ mole l.$^{-1}$; $[X]_0 = 6{\cdot}6 \times 10^{-3}$ mole l.$^{-1}$. (*c*) $[M]_0 = 0{\cdot}32$ mole l.$^{-1}$; $[X]_0 = 2{\cdot}15 \times 10^{-3}$ mole l.$^{-1}$.



derivative, polymer is precipitated and remains suspended during the reaction represented by *CD*; after *D* has been passed the precipitate consolidates.

The rate coefficient corresponding to the portion of the curve between *B* and *C* in Fig. 2(*c*) is 2·9 mole^{-1} l. min.$^{-1}$. This is a reasonable value for the normal propagation reaction (1) and may be compared to that for α-*N*-carboxy-DL-phenylalanine anhydride,[1] *viz.*, 0·94 mole^{-1} l. min.$^{-1}$. The corresponding values deduced from Figs. 3(*a*) and 4(*a*) referring to polymerizations in benzene are 3·8 and 3·0 mole^{-1} l. min.$^{-1}$, respectively.

(iii) α-N-*Carboxy*-L-*leucine Anhydride in Nitrobenzene.*—Using concentrations of this anhydride in nitrobenzene similar to those reported by Lundberg and Doty,[4] we found no difficulty in reproducing their results. A typical experiment is shown in Fig. 4(*b*). In this case also the relative sizes of the various steps were found to depend on the concentrations of anhydride and base used; Fig. 4(*c*) shows that with rather high initial concentrations the *BC* stage is very small.

(iv) α-N-*Carboxy*-L-*proline Anhydride in Nitrobenzene.*—The polymerization of α-*N*-carboxy-L-proline anhydride initiated by *n*-hexylamine in nitrobenzene solution [Fig. 3(*b*)]

shows the characteristic features associated with the polymerization of other anhydrides which form sparingly soluble polymers. Poly-L-proline separates at an early stage, and the rate of reaction subsequently increases by a factor of approximately 1·9 in the experiment illustrated. Towards the end of the reaction a decrease in the velocity coefficient occurs.

(v) *General Conclusions.*—The experiments described lead to the following conclusions. (*a*) Increases in the velocity coefficient during polymerization are commonly encountered when the polypeptide product is precipitated; the increase coincides approximately with the appearance of visible heterogeneity. (*b*) Similar results are obtained with *N*-substituted and unsubstituted anhydrides. (*c*) With unsubstituted anhydrides the main increase in rate can occur when a mean degree of polymerization as low as **3** or **4** has been reached [point *C*, Figs. **1**, **2**(*c*), and **3**(*a*)]. This value is too low to permit the growing chains to adopt the α-helical configuration since the α-helix contains close to 3·6 residues per turn. It may be argued that a small fraction of the chains at the points *C* [Figs. **1**, **2**(*c*), and **3**(*a*)] will be α-helical on account of the spread in molecular weights; if this were the cause of the acceleration the latter should continue to a very marked extent considerably beyond *C*. However, the acceleration is substantially complete by the time the chains have reached a degree of polymerization of five; it is unlikely that they are completely α-helical at this stage. Idelson and Blout [5] suggested that the terminal base groups of low polymers of γ-benzyl esters of L-glutamic acid may be less accessible, and therefore react more slowly, than those of the α-polymer. In principle this could arise if the low polymers were associated by inter-chain hydrogen bonds. A mechanism of this kind cannot apply to *N*-substituted polymers, and, in view of (*b*) above, is unlikely to be important in general. Further, it is difficult to believe that the terminal groups are less accessible in solution than in the precipitated polymer. The acceleration is not a function merely of the nature of the solvent alone, since, for example, α-*N*-carboxysarcosine anhydride at constant carbon dioxide pressure polymerizes normally in nitrobenzene whereas the *N*-carboxy-anhydrides of L-leucine and L-proline give accelerating reactions in this medium.

It appears to us that the increase in rate observed at the points *C* in Figs. **1**—**4** must have its origin in the development of heterogeneity, which seems to be the only common feature in the systems studied. In view of these observations it is debatable whether there is any evidence for a dependence of the propagation rate on a specific chain configuration. Such evidence could only be obtained from strictly homogeneous polymerizations, and to reach a decision further work is required; however, in our experience polymerizatons of this kind can be described by a single propagation coefficient. [For example, we have confirmed the findings of Lundberg and Doty [4] that in highly purified *NN*-dimethylformamide the (homogeneous) polymerization of α-*N*-carboxy-L-glutamic anhydride γ-benzyl ester is of strictly first order throughout its whole course.] Most of the evidence cited in favour of such a dependence is derived from work on the γ-benzyl ester anhydride in dioxan. It is possible that the polymerization of this anhydride is markedly affected by the presence of trace impurities which can affect the precipitation of the polymer. Indeed, Lundberg and Doty [4] have recorded that impurities can influence the physical state of solution of this polymer.

The *N*-carboxy-anhydrides, like the polypeptides, are highly polar substances, and it is reasonable to suppose that they are preferentially soluble in a phase consisting of swollen polypeptide in contact with a poor solvent for the polymer. Since the reactive base residues are attached to the polymer chains, precipitation followed by absorption of the anhydride will increase the effective concentration of both reactants and so lead to an increase in the rate of reaction. Although the chains may be immobilised in such an aggregate, the small monomer molecules are comparatively mobile. In order that this mechanism alone should result in a large increase in the velocity it is necessary that the volume of the anhydride-rich precipitated phase should be small compared with the total liquid volume. This appears to be the case in the systems described above. However,

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the high dielectric constant of the swollen phase may be an additional factor tending to increase the rate of reaction.

An alternative, though somewhat similar, mechanism may be visualised in which the anhydride molecules are reversibly adsorbed on the precipitated polymer molecules, and then react particularly readily on account of the proximity of the base at the end of the chains and possible activation arising from the adsorption. It is not clear whether any specific conformation of the end portions of the chains would be required to produce this enhancement in rate, but the observation that anhydrides of different structure behave similarly make this seem rather unlikely. This mechanism has analogies with the chain-effect encountered in homogeneous polymerizations initiated by polysarcosine,[13] the adsorption of anhydride by the precipitated polymer taking the place of the attachment of anhydride molecules to polysarcosine by hydrogen bonds.

Phenomena of the type considered above will generally affect the nature of the molecular-weight distribution, and will lead to departures from the Poisson distribution expected for homogeneous polymerization. The result will be a broadening of the distribution; this has been observed by Mitchell, Woodward, and Doty [7] in the case of the γ-benzyl ester of *N*-carboxy-L-glutamic anhydride, and was previously interpreted [4] in terms of the two-stage propagation suggested by Doty and Lundberg.[3]

COURTAULDS, LIMITED, RESEARCH LABORATORY,
MAIDENHEAD, BERKS.

[*Received, August 25th*, 1958.]

[13] Ballard and Bamford, *Proc. Roy. Soc.*, 1956, *A*, **236**, 384.

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213. *The Structures of Two Acids from Olive Leaves.*

By G. D. MEAKINS and R. SWINDELLS.

Two acids from olive leaves have been identified as 10 : 16-dihydroxyhexadecanoic and 9 : 10 : 18-trihydroxyoctadecanoic acid.

M. PASSERINI and his collaborators isolated two apparently new acids from leaves of the olive (*Olea europaea*) [1,2] and of Japanese privet (*Ligustrum japonicum*).[3] These acids, designated I and II, were separated by fractional precipitation of the sodium salts [1] or by fractional crystallisation of the acids after preliminary purification with baryta. Microanalytical data on the acids I and II and their methyl esters indicated formulæ $C_{14}H_{28}O_4$ and $C_{15}H_{30}O_4$ respectively, but no structural investigations were carried out.

Working with olive leaves we separated the acids I and II efficiently by chromatography of the mixed methyl esters on alumina. The constants of the acids and their derivatives (see Table) suggested that they might be identical with previously known compounds, isolated for example from the cutin of *Agave americana*.[4] Proof that acid I is 9 : 10 : 18-trihydroxyoctadecanoic acid (I; R = H, $C_{18}H_{36}O_5$) and acid II is 10 : 16-dihydroxyhexadecanoic acid (II; R = H, $C_{16}H_{32}O_4$) was obtained by slight modifications of the methods used by Matic with the hydroxy-acids from *Agave* cutin.[4]

Acid I (I; R = H) on reduction with phosphorus and hydriodic acid, followed by zinc and hydrochloric acid in methanol, gave methyl stearate (III; $n = 16$). Chromic oxidation of the methyl ester I (I; R = Me) in acetone at 20° produced the 9 : 10-dioxo-compound (IV). Fission of the methyl ester (I; R = Me) with chromic oxide in acetic acid at 40° afforded azelaic acid and its monomethyl ester (VI; R = H and Me) which were separated with pentane and methylated to products identified in both cases as

[1] Passerini, Ridi, and Ceccherelli, *Sperimentale, Sez. Chim. biol.*, 1951, **2**, 63.
[2] Passerini, Ridi, and Papini, *Ann. Chim.* (*Italy*), 1953, **43**, 201.
[3] Passerini and Papini, *Sperimentale, Sez. Chim. biol.*, 1951, **2**, 72; *Ann. Chim.* (*Italy*), 1953, **43**, 204.
[4] Matic, *Biochem. J.*, 1956, **63**, 168.

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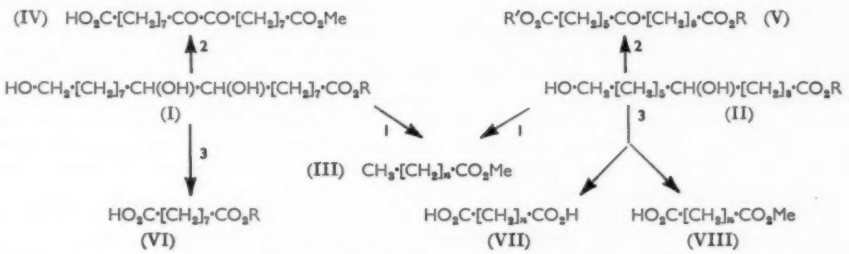
dimethyl azelate by vapour-phase chromatography. [In the present work vapour-phase chromatography of methyl esters [5] was convenient for characterising various oxidation and reduction products of acids I and II. Mixtures of esters $MeO_2C\cdot[CH_2]_n\cdot CO_2Me$ with $n = 4$—8 gave separate peaks whose times of emergence and areas allowed semiquantitative analyses to be made.]



Reagents: 1, HI–P, then Zn–HCl–MeOH. 2, CrO_3–Me_2CO at 20°. 3, CrO_3–AcOH at 40°.

Reduction of acid II (II; R = H) gave methyl palmitate (III; $n = 14$), and mild oxidation of methyl ester II (II; R = Me) afforded the 7-oxo-ester (V; R = Me, R′ = H) which was converted into the diester (V; R = R′ = Me) and the diacid (V; R = R′ = H). Fission of the ester (II; R = Me) yielded adipic and pimelic acid (VII; $n = 4$ and 5) and the monoesters of azelaic and sebacic acids (VIII; $n = 7$ and 8). A sample of 10 : 16-dihydroxyhexadecanoic acid kindly supplied by Dr. M. Matic was converted into the methyl ester and the 7-oxo-compounds (V); mixed melting points with derivatives prepared from acid II showed no depression. There is no obvious explanation for the one case of melting point discrepancy, *viz.*, that for the parent acids.

Melting points of hydroxy-acids and derivatives.

	Acid I [1,2]	9 : 10 : 18-Trihydroxy-octadecanoic acid [4]	Present work
Acid	100—102°	102—103°	99—102°
Methyl ester	81—82	81—82	80—82
	Acid II	10 : 16-Dihydroxy-hexadecanoic acid	
Acid	95—97	75—76	95—98
Methyl ester	73—75	67·5—68·3	68—69
7-Oxo-diacid (V; R = R′ = H)	—	112·5—113·5	110—112
,, monomethyl ester (V; R = Me, R′ = H)	—	64—66 *	64—66
,, dimethyl ester (V; R = R′ = Me)	—	39—43 *	40—43

* Prepared from 10 : 16-dihydroxyhexadecanoic acid kindly supplied by Dr. M. Matic.

Experimental

M. p.s were determined on a Kofler block and are corrected. Neutral alumina was prepared by stirring Peter Spence material (grade H) with an excess of ethyl acetate at 20° for 2 days, filtration, washing repeatedly with hot water, and heating at 250° for 2 days. Vapour-phase chromatography was carried out on a Griffin (mark 2) apparatus using a column (6′ × 0·25″) packed with Celite impregnated with Silicone (Griffin and George " S.E.30 "): with the column temperatures specified below and a constant nitrogen flow rate (2·1 l./hr.) the times of emergence were characteristic of the various compounds examined.

Isolation of Acids from Olive Leaves.—Dry leaves (200 g.) were minced and stirred with boiling 5% aqueous sodium hydroxide (2 l.) for 30 min. The cooled mixture was filtered through muslin and then through Whatman's No. 541 filter paper. After acidification of the

[5] James and Martin, *ibid.*, p. 144.

filtrate with 4N-hydrochloric acid the insoluble material was isolated by centrifugation, washed with water, dried, and continuously extracted with ether for 12 hr. Evaporation of the ether afforded a dark green gum (*ca.* 18 g.) which was shaken with 5% aqueous sodium carbonate (1 l.). The mixture was washed with ether (2 × 500 c.c.), warmed (to remove ether), cooled, and acidified with 4N-hydrochloric acid. The material collected by filtration was washed and dried to give a pale green solid (*ca.* 16 g.).

A portion of the above solid (5 g.) was treated with an excess of diazomethane in ether. The solution was concentrated and adsorbed on neutral alumina (300 g.). Elution with ether (500 c.c.) gave a green oil which was discarded. Further elution with ether (1·5 l.) afforded a solid (1·4 g.) which crystallised from light petroleum–ethyl acetate to give methyl 10 : 16-dihydroxyhexadecanoate (II; R = Me) (1·1 g.) as white needles, m. p. 68—69° (Found: C, 67·45; H, 11·05. Calc. for $C_{17}H_{34}O_4$: C, 67·5; H, 11·25%), $\nu_{max.}$ (in $CHCl_3$) 3625, 3450, 1730, and 1047 cm.$^{-1}$. Hydrolysis with ethanolic potassium hydroxide yielded 10 : 16-dihydroxyhexadecanoic acid (II; R = H), m. p. 95—98° (from aqueous methanol) (Found: C, 66·6; H, 11·25. Calc. for $C_{16}H_{32}O_4$: C, 66·6; H, 11·1%).

Elution with ether–methanol (9 : 1) gave a green gum which was rejected, followed by solid material (1·2 g.). Crystallisation of this from light petroleum–ethyl acetate afforded material (1 g.; m. p. 73—75°) which was hydrolysed with ethanolic potassium hydroxide. The product crystallised from acetone–chloroform and then from methanol, to give 9 : 10 : 18-trihydroxyoctadecanoic acid (I; R = H) (0·8 g.), m. p. 99—102° (Found: C, 65·0; H, 10·9. Calc. for $C_{18}H_{36}O_5$: C, 65·0; H, 10·85%). Treatment of the acid in ether–methanol with ethereal diazomethane afforded the methyl ester (I; R = Me), m. p. 80—82° after crystallisation from light petroleum–ethyl acetate (Found: C, 66·0; H, 11·05. Calc. for $C_{19}H_{38}O_5$: C, 65·9; H, 11·0%), $\nu_{max.}$ (in $CHCl_3$) 3610, 3430, 1724, and 1050 cm.$^{-1}$.

Reduction of Acids (I and II; R = H).—The acid (200 mg.) was refluxed with hydriodic acid (*d* 1·7; 6 c.c.) and red phosphorus (70 mg.) for 16 hr. After dilution with water and extraction with ether, the ether solution was washed with 5% aqueous sodium hydrogen sulphite, dried, and evaporated. The product was dissolved in methanol (10 c.c.) and boiled with 10N-hydrochloric acid (2 c.c.) and zinc (300 mg.) for 6 hr. Filtration, dilution with water, and extraction with ether afforded the methyl ester of the appropriate fatty acid. 9 : 10 : 18-Trihydroxyoctadecanoic acid gave methyl stearate (150 mg.), m. p. 36—38° (from acetone) (time of emergence 190 min. from vapour-phase chromatography column at 190°). This ester was hydrolysed to stearic acid, m. p. and mixed m. p. 67—69°. 10 : 16-Dihydroxyhexadecanoic acid gave methyl palmitate (170 mg.) (time of emergence 140 min. at 190°), which was hydrolysed to palmitic acid, m. p. and mixed m. p. 60—63°.

Oxidation of Methyl Esters (I and II; R = Me).—(a) *With chromic acid in acetone.* The methyl ester (400 mg.) in acetone (25 c.c.) was treated with a slight excess of 8N-chromic acid at 20°. After dilution with water the product was isolated with ether in the usual way. Oxidation of methyl 9 : 10 : 18-trihydroxyoctadecanoate for 2 min. gave the *methyl hydrogen* 9 : 10-*dioxo-octadecanedioate* (IV), yellow plates (85 mg.), m. p. 80—83° (from ethyl acetate) (Found: C, 63·7; H, 8·95. $C_{19}H_{32}O_6$ requires C, 64·05; H, 9·0%), $\nu_{max.}$ (in CCl_4) 3000 (very broad), 1738, and 1709 cm.$^{-1}$. Azelaic acid (100 mg.), m. p. 103—106°, was isolated from the ethyl acetate mother-liquor.

Oxidation of methyl 10 : 16-dihydroxyhexadecanoate for 5 min. gave the 16-*methyl hydrogen* 7-*oxohexadecanedioate* (V; R = Me, R′ = H), plates (240 mg.), m. p. 64—66° (from ethyl acetate) (Found: C, 65·2; H, 9·75. $C_{17}H_{30}O_5$ requires C, 65·0; H, 9·55%), $\nu_{max.}$ (in CCl_4) 3000 (very broad), 1740, and 1710 cm.$^{-1}$. Treatment of the ester with an excess of diazomethane afforded *dimethyl* 7-*oxohexadecanedioate* (V; R = R′ = Me), m. p. 40—43° (Found: C, 65·6; H, 9·5. $C_{19}H_{32}O_5$ requires C, 65·8; H, 9·75%), $\nu_{max.}$ (in CCl_4) 1739, and 1708 cm.$^{-1}$. Saponification of both esters gave 7-oxohexadecanedioic acid (V; R = R′ = Me), m. p. 110—112° (Found: C, 64·2; H, 9·35. Calc. for $C_{16}H_{28}O_5$: C, 64·0; H, 9·4%).

(b) *With chromic oxide in acetic acid.* The ester (70 mg.) and chromic acid (90 mg.) were dissolved in acetic acid (3 c.c.), and the solution was kept at 40° for 24 hr. The product obtained after dilution with water and thorough extraction with ether was refluxed with pentane (25 c.c.) and then cooled. Two fractions ("pentane-insoluble" and "pentane-soluble") were obtained, and separately methylated with diazomethane. Methyl 9 : 10 : 18-trihydroxyoctadecanoate afforded dimethyl azelate (time of emergence 29 min. from column at 177°) in both fractions. Methyl 10 : 16-dihydroxyhexadecanoate gave dimethyl adipate

and dimethyl pimelate (times of emergence 8 min. and 12·5 min. respectively) from the pentane-insoluble fraction, and dimethyl azelate and dimethyl sebacate (times of emergence 29 min. and 44 min. respectively) from the pentane-soluble fraction.

These emergence times agree with those found with authentic specimens: dimethyl suberate emerges after 18·5 min.

We are indebted to Professor F. Sondheimer (Weizmann Institute, Rehovoth) and Mr. E. S. Tonna (Civil Defence School, Malta) for supplying the olive leaves, and to the Department of Scientific and Industrial Research for a grant (to R. S.).

THE UNIVERSITY, MANCHESTER, 13. [*Received, October 17th*, 1958.]

214. *Ligand-field Splittings due to Organic Amines, Phosphines, Arsines, Sulphides, Selenides, and Tellurides.*

By J. CHATT, G. A. GAMLEN, and L. E. ORGEL.

The ultraviolet and visible spectra of a series of complexes of the type *trans*-[L,piperidinePtCl$_2$] have been measured. In these the ligands L are aliphatic amines, phosphines, etc. Their ligand-field splittings, inferred from the energies of the $d_{xy} \longrightarrow d_{x^2-y^2}$ transition, decrease in the sequence $P(OMe)_3 > PPr^n_3 > piperidine > AsPr^n_3 > Et_2S > Et_2Se > Et_2Te$. This is unlikely to be a universal sequence but will depend to some extent on the π-bonding capacities of the metals. The total range of energy of the transitions is small, varying from 33,400 cm.$^{-1}$ in the $P(OMe)_3$ compound to 29,400 cm.$^{-1}$ in its Et_2Te analogue.

Spectra.—While a great deal of information is available concerning the crystal- or ligand-field splittings (Δ) produced by oxygen- and nitrogen-containing ligands, virtually nothing has been written about the corresponding splittings in phosphine, arsine, sulphide, selenide, and telluride complexes. Here we interpret the ligand-field bands in the spectra of a series of planar complexes of the type *trans*-[L,piperidinePtCl$_2$] (Figs. 1—3). In Fig. 4 we reproduce three related spectra which are relevant to the present work.

Interpretation.—In the Table are listed the values of $\lambda_{max.}$, the energy E, and $\varepsilon_{max.}$ for what we believe to be the first spin-allowed transition. This assignment is based on a previous study of the spectra of the platinous chloro-ammines,[1] and the transition is probably that which is predominantly $d_{xy} \longrightarrow d_{x^2-y^2}$. The total range of energy of this transition is seen to be quite small, the $d_{xy} \longrightarrow d_{x^2-y^2}$ transition frequency varying from 33,400 cm.$^{-1}$ in the $P(OMe)_3$ compound to 29,400 cm.$^{-1}$ in the Et_2Te compound. The intensities are undoubtedly substantially higher in these compounds than in the chloro-ammines, but the values given are not very significant, since we have not carried out Gaussian analyses of the spectra.

Wavelength $\lambda_{max.}$, energy E, and intensity $\varepsilon_{max.}$ of the first spin-allowed transition in the complex trans-[L,piperidinePtCl$_2$].

L	$\lambda_{max.}$ (mμ)	E (cm.$^{-1}$)	$\varepsilon_{max.}$	L	$\lambda_{max.}$ (mμ)	E (cm.$^{-1}$)	$\varepsilon_{max.}$
Piperidine	315	31,750	78	Et_2S	330	30,300	136
$P(OMe)_3$	299	33,400	319	Et_2Se	335	29,850	160
PPr^n_3	307	32,600	303	Et_2Te	340	29,400	350
$AsPr^n_3$	321	31,150	310				

Before we draw deductions from these results about the ligand-field splittings in other complexes there are two problems to be considered. First, there is the special problem of extrapolating from planar to octahedral complexes and, secondly, the more general

[1] Chatt, Gamlen, and Orgel, *J.*, 1958, 486.

FIG. 1.

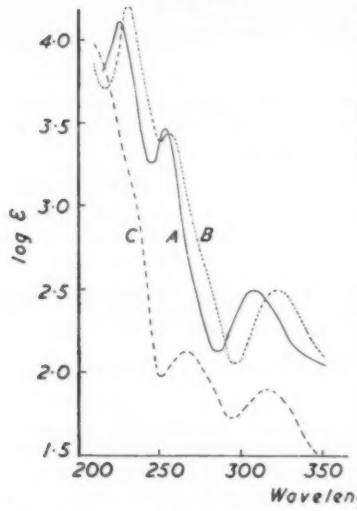


FIG. 2.

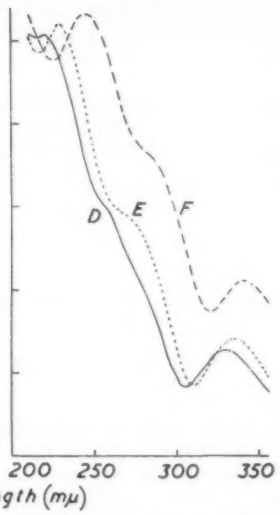


FIG. 1. *Ultraviolet spectra of* (*A*) *trans*-[PPr^n_3,pipPtCl$_2$], (*B*) *trans*-[$AsPr^n_3$,pipPtCl$_2$], *and* (*C*) *trans*-[pip$_2$PtCl$_2$].

FIG. 2. *Ultraviolet spectra of* (*D*) *trans*-[Et_2S,pipCl$_2$], (*E*) *trans*-[Et_2Se,pipPtCl$_2$], *and* (*F*) *trans*-[Et_2Te,pipPtCl$_2$].

FIG. 3.

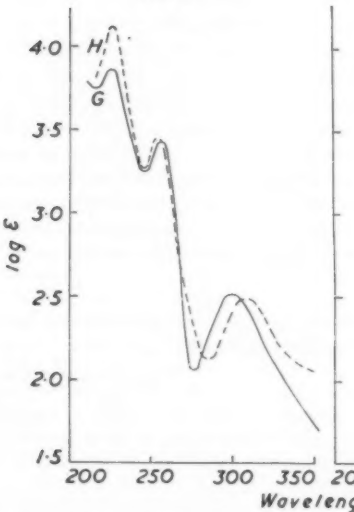


FIG. 4.

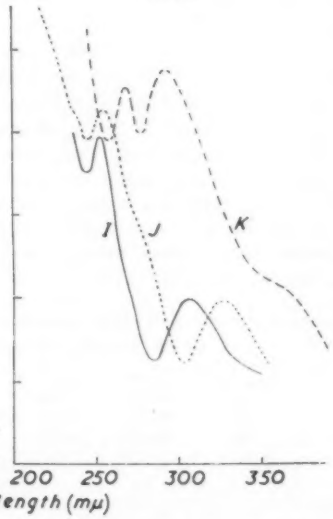


FIG. 3. *Ultraviolet spectra of* (*G*) *trans*-[$P(OMe)_3$,pipPtCl$_2$] *and* (*H*) *trans*-[PPr^n_3,pipPtCl$_2$].

FIG. 4. *Ultraviolet spectra of* (*I*) *trans*-[PPr^n_3,pipPtCl$_2$], (*J*) *trans*-[PPr^n_3,pipPtBr$_2$], *and* (*K*) *trans*-[PPr^n_3,pipPtI$_2$].

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problem of telling how the relative sizes of the splitting produced by different ligands vary from one metal ion to another.

Fortunately the $d_{xy} \longrightarrow d_{x^2-y^2}$ transition is the one most closely related to the $t_2 \longrightarrow e$ transition (*i.e.*, $d_{xy},d_{yz},d_{zx} \longrightarrow d_{x^2-y^2},d_{z^2}$) of an octahedral complex, because the non-cubic component of the ligand field in a square complex to a first approximation affects the d_{xy} and the $d_{x^2-y^2}$ orbitals equally. The values of E in the Table differ from the energy separation between the $d_{x^2-y^2}$ and the d_{xy} orbitals by an electrostatic energy term which should not vary much from compound to compound.[1] For this reason the results presented probably give reliable information about relative Δ values also for octahedral complexes.

We believe that the fact that Δ is larger for phosphines than for amines indicates that double bonding is important in the former,[2] *i.e.*, that the larger d_{xy}–$d_{x^2-y^2}$ separation is due to the stabilisation of the d_{xy}-orbital by π-bonding rather than the destabilisation of the $d_{x^2-y^2}$-orbital by σ-bonding. This suggestion is supported by the larger separation in the $P(OMe)_3$ than in the PPr^n_3 complex. Presumably the former ligand forms weaker σ- and stronger π-bonds to the Pt^{++} ion and the latter effect is more important than the former.

If we accept this explanation then it is clear that the relative value of Δ for phosphines, etc., compared with that for aliphatic amines must decrease as the d_π donor property of the metal decreases. Thus the order, $P(OMe)_3 > PPr^n_3 >$ piperidine $> AsPr^n_3 > Et_2S > Et_2Se > Et_2Te$, can only be expected to hold for complexes to transition metals in relatively low valencies. In complexes of higher valency the *relative* Δ values for simple amines would increase while in zero-valent compounds it would decrease still further. Nevertheless, it appears that for the heavier ligand atoms in analogous complexes the ligand-field splittings will normally decrease as each Group is ascended, *i.e.*, P > As; S > Se > Te; Cl > Br > I.

The shift of the $d \longrightarrow d$ transitions to lower energy in bromide and iodide complexes relative to that in the chloride complex (Fig. 4) is consistent with the lower Δ values usually found for the heavier halogens.

The intense bands usually beyond 240 mμ we believe to be connected with charge transfer and $d \longrightarrow p$ transitions.

Experimental.—Platinum complexes. The preparation and analysis of the substances used in these experiments have been described by Chatt, Duncanson, and Venanzi.[3]

Measurement of the absorption spectra. These were determined on a Unicam S.P. 500 spectrophotometer modified to take 10 cm. cells,[4] with *n*-hexane " Special for Spectroscopy " as solvent. The solutions were accurately prepared to be about 10^{-3}M, and the spectra measured at 23° ± 1°.

The authors gratefully acknowledge the experimental assistance of Messrs. D. H. Goschenhofer, D. T. Rosevear, and M. L. Searle.

Imperial Chemical Industries Limited,
Akers Research Laboratories,
The Frythe, Welwyn, Herts. [*Received, November 5th*, 1958.]

[2] Cf. Chatt, Duncanson, and Venanzi, *J.*, 1958, 3203, and references therein.
[3] Chatt and Venanzi, *J.*, 1955, 3858; Chatt, Duncanson, and Venanzi, *J.*, 1955, 4461.
[4] Gamlen, Photoelectric Spectrometry Group Bulletin No. 11, 1958, 286.

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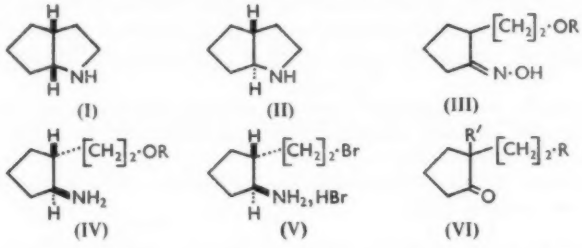
215. *Synthetic and Stereochemical Investigations of Reduced Cyclic Bases. Part VII.* The Synthesis of* cis- *and* trans-2 : 3-*cyclo*-*Pentanopyrrolidine.*

By H. Booth, F. E. King, K. G. Mason, J. Parrick, and R. L. St. D. Whitehead.

Both *cis*- and *trans*-2 : 3-*cyclo*pentanopyrrolidine have been synthesised [1] and the identity of the base hitherto tentatively regarded as the *trans*-isomer [2] has been confirmed.

cis- and *trans*-2 : 3-*cyclo*-Pentanopyrrolidine (I and II respectively) are of stereochemical interest in view of the strain in the *trans*-fused five-membered rings. The only recorded preparative work in the *cyclo*pentanopyrrolidine series was by Prelog and Szpilfogel,[2] who reduced the oxime (III; R = Ph) with sodium and ethanol or catalytically with platinum oxide in ethanol to an amine (IV; R = Ph) to which they assigned the *trans*-configuration. Attempts to prepare its stereoisomer by reduction of the oxime in acid solution were unsuccessful. When the amine (IV; R = Ph) was heated with hydrobromic acid, a bromo-amine hydrobromide (V) was produced, and cyclisation with alkali then yielded the presumed *trans*-2 : 3-*cyclo*-pentanopyrrolidine (II).



cis- and *trans*-2 : 3-*cyclo*Pentanopyrrolidine have now been synthesised as follows.

First, 2-iodoethyl acetate was condensed with the sodium derivative of ethyl 2-oxo-*cyclo*pentanecarboxylate in benzene. The resulting keto-ester (VI; R = OAc, R′ = CO_2Et) was hydrolysed smoothly with dilute sulphuric acid to the hydroxy-ketone (VI; R = OH, R′ = H). When concentrated hydrochloric or hydrobromic acid was used as the hydrolytic agent, the product was the chloro- or bromo-ketone (VI; R = Cl or Br, R′ = H). The hydroxy-ketone was converted into the oxime (III; R = H) which was reduced with sodium in boiling ethanol to the crystalline *trans*-2-2′-hydroxyethyl*cyclo*-pentylamine (IV; R = H), the configuration appearing to follow from its production under alkaline conditions. Treatment of the base with hydrobromic acid afforded the bromo-amine hydrobromide (V), which was cyclised with aqueous alkali to a 2 : 3-*cyclo*-pentanopyrrolidine identical with that prepared by Prelog and Szpilfogel.[2]

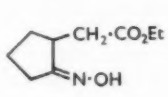
Attempts to prepare the geometrical isomer of (IV; R = H) by reduction of the oxime (III; R = H) in acetic acid with sodium amalgam, or in acetic anhydride with zinc dust, were unsuccessful. Application of the Leuckardt reaction, which usually gives a preponderance of the *cis*-isomer, to the ketone (VI; R = OH, R′ = H) resulted in a mixture containing at least 70% of the amine (IV) already prepared. However, when the oxime-ester (VII) was hydrogenated over Raney nickel the product consisted of ethyl *trans*-2-amino*cyclo*pentylacetate (VIII), *cis*-2 : 3-*cyclo*pentanopyrrolid-5-one (IX), and the secondary amine (X), which were separated by distillation.

* Part VI, Booth and King, *J.*, 1958, 2688.

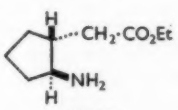
[1] Cf. Booth, King, Parrick, and Whitehead, *Chem. and Ind.*, 1956, 466.

[2] Prelog and Szpilfogel, *Helv. Chim. Acta*, 1945, **28**, 178.

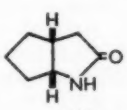
The *trans*-configuration of the ester (VIII) was evident from its resistance to cyclisation, it being recovered unchanged after 24 hours' refluxing in benzene and polymerised when heated for 2 hr. at 140°. This behaviour contrasts with that of methyl *trans*-2-amino*cyclo*hexylacetate, from which the corresponding lactam, *trans*-octahydro-2-oxoindole [3] is obtained without difficulty.



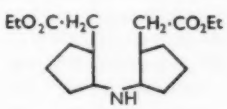
(VII)



(VIII)



(IX)



(X)

Hydrolysis of the amino-ester (VIII) and of the lactam (IX) with dilute hydrochloric acid gave two different amino-acids, and accordingly the lactam must have the *cis*-configuration. *cis*-2 : 3-*cyclo*Pentanopyrrolidine was then prepared by reducing the lactam (IX) with lithium aluminium hydride. When the *trans*-amino-ester (VIII) was treated with lithium aluminium hydride, an amino-alcohol identical with (IV; R = H) was isolated, thus confirming the configuration attributed to this amino-alcohol and of the *cyclo*pentanopyrrolidine prepared by ring-closure of the bromo-amine hydrobromide (V).

Measurements of the principal physical constants of the two *cyclo*pentanopyrrolidines show that the *trans*-base has the higher b. p. and refractive index, but the lower density. The qualitative effect of stereochemical differences on these constants, formerly stated in the Auwers–Skita rule, is now more accurately expressed by Allinger's generalisation [4] that the higher values are attributable to the less stable configuration. Since the *trans*-*cyclo*pentanopyrrolidine is the less stable owing to the greater strain inherent in the *trans*-configuration, the rule is confirmed in respect of b. p. and refractive index, but not of density. In the analogous 3-oxa- and 3-thia-*bicyclo*[3 : 3 : 0]octane series also it is the *trans*-isomers which have the higher b. p.s and refractive indexes.[5,6] The densities of the oxa*bicyclo*octanes have not been recorded, and those of the *cis*- and *trans*-thia*bicyclo*-octanes were measured at different temperatures, but the published figures (*cis*, d^{20} 1·0427, d^{25} 1·0386: *trans*, d^{30} 1·0294) suggest that under comparable conditions the value for the *cis*-thia*bicyclo*octane, as with the *cyclo*pentanopyrrolidines, may again be the greater.

Preliminary work was carried out on an alternative synthesis of *cis*-2 : 3-*cyclo*pentanopyrrolidine. It used 2-2′-nitroethyl*cyclo*pentanone which was hydrogenated in methanol over Raney nickel. The filtered solution, which presumably contained a *cyclo*pentenopyrrolidine (cf. King, Bovey, Mason, and Whitehead [7]), was treated with sodium and boiling ethanol: a poor yield of *cis*-2 : 3-*cyclo*pentanopyrrolidine was obtained.

Experimental

Ethyl 1-2′-*acetoxyethyl*-2-*oxo*cyclo*pentanecarboxylate* (VI; R = OAc, R′ = CO_2Et).—Ethyl 2-oxo*cyclo*pentanecarboxylate (150 g.) was added to a suspension of powdered sodium (23 g.) in benzene (1 l.), and the mixture was heated under reflux for 2 hr. The cooled mixture was treated with freshly distilled 2-iodoethyl acetate (230 g.), and refluxing was continued for 4 days. The resulting solution was poured into 2% hydrochloric acid, and the benzene layer was separated, dried, and evaporated. Distillation yielded the *keto-ester* (145 g., 62%), b. p. 175—177°/16 mm. (Found: C, 60·1; H, 7·4. $C_{12}H_{18}O_5$ requires C, 59·7; H, 7·4%). The *semicarbazone* had m. p. 110° (from light petroleum–ethyl acetate) (Found: C, 52·15; H, 6·9; N, 14·2. $C_{13}H_{21}O_5N_3$ requires C, 52·15; H, 7·0; N, 14·0%).

2-2′-*Bromoethyl*cyclo*pentanone*.—The foregoing keto-ester (29·2 g.) was heated under reflux

[3] Booth and King, *J.*, 1958, 2688.
[4] Allinger, *Experientia*, 1954, **10**, 328.
[5] Owen and Peto, *J.*, 1955, 2383.
[6] Birch, Dean, Hunter, and Whitehead, *J. Org. Chem.*, 1955, **20**, 1178.
[7] King, Bovey, Mason, and Whitehead, *J.*, 1953, 250.

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for 5 hr. with 30% hydrobromic acid (120 c.c.). The mixture was neutralised with sodium carbonate solution and extracted with ether. Evaporation of the dried ethereal extracts yielded an oil which was distilled. After a small forerun (1·2 g.), b. p. 56°/14 mm., the bromo-ketone (9·1 g., 40%) distilled at 116°/14 mm. The *semicarbazone* crystallised from ethanol–acetic acid in needles, m. p. 158° (decomp.) (Found: C, 38·4; H, 5·7; N, 16·8. $C_8H_{14}ON_3Br$ requires C, 38·7; H, 5·7; N, 16·9%). The 2 : 4-*dinitrophenylhydrazone* crystallised from acetic acid in yellow prisms, m. p. 156° (Found: C, 42·2; H, 4·1; N, 15·0. $C_{13}H_{15}O_4N_4Br$ requires C, 42·1; H, 4·0; N, 15·1%).

2-2′-*Chloroethyl*cyclo*pentanone*.—Hydrolysis of the keto-ester (6 g.) with (32%) hydrochloric acid (25 c.c.) for 7 hr. and working up as described above for the bromo-compound gave the chloro-ketone (1·8 g., 50%), b. p. 98—100°/10 mm. This yielded a *semicarbazone*, needles (from ethanol), m. p. 180° (decomp.) (Found: C, 47·6; H, 7·2; N, 20·4; Cl, 17·6. $C_8H_{14}ON_3Cl$ requires C, 47·3; H, 6·9; N, 20·6; Cl, 17·4%), and a 2 : 4-*dinitrophenylhydrazone*, plates (from acetic acid), m. p. 158° (Found: C, 47·7; H, 5·0; N, 17·5. $C_{13}H_{15}O_4N_4Cl$ requires C, 47·8; H, 4·6; N, 17·1%).

2-2′-*Hydroxyethyl*cyclo*pentanone*.—Ethyl 1-2′-acetoxyethyl-2-oxo*cyclo*pentanecarboxylate (63·5 g.) was treated with 10% sulphuric acid (250 c.c.), and the mixture was refluxed for 1½ hr. The cooled solution was neutralised with concentrated aqueous ammonia and evaporated under reduced pressure until solid separated. Extraction with ether then afforded the hydroxy-ketone (20 g., 59%), b. p. 127—130°/14 mm. The *semicarbazone* crystallised from ethyl acetate in needles, m. p. 157° (Found: C, 52·0; H, 8·0; N, 22·4. $C_8H_{15}O_2N_3$ requires C, 51·9; H, 8·1; N, 22·7%), and the 2 : 4-*dinitrophenylhydrazone* from ethanol in orange needles, m. p. 174—176° (Found: C, 50·6; H, 5·5; N, 18·2. $C_{13}H_{16}O_5N_4$ requires C, 50·6; H, 5·2; N, 18·2%).

2-2′-*Acetoxyethyl*cyclo*pentanone*.—The hydroxy-ketone (6 g.) was heated under reflux with acetic anhydride (30 c.c.) and fused sodium acetate (8 g.). After the usual working-up, the acetoxy-ketone (6 g., 75%) was obtained as an oil, b. p. 128°/15 mm. [*semicarbazone*, needles (from ethanol), m. p. 151° (Found: C, 53·1; H, 7·4; N, 18·2. $C_{10}H_{17}O_3N_3$ requires C, 53·1; H, 7·5; N, 18·4%)]. The acetoxy-ketone with 2 : 4-dinitrophenylhydrazine sulphate in methanol (" Brady's reagent ") gave the derivative of the hydroxy-ketone; this had m. p. and mixed m. p. 175° (Found: 17·7. Calc. for $C_{13}H_{16}O_5N_4$: N, 18·2%).

2-2′-*Hydroxyethyl*cyclo*pentanone Oxime*.—The hydroxy-ketone (12·8 g.) was dissolved in moist ether (50 c.c.), and an intimate mixture of hydroxylamine hydrochloride (14 g.) and sodium hydrogen carbonate (20 g.) was added. After the mixture had been warmed on the water-bath for 3 hr., the ether was separated, dried, and evaporated. Distillation of the residue afforded the *oxime* (12·6 g., 88%), b. p. 183—185°/20 mm. Crystallisation from ethyl acetate gave octahedra, m. p. 84° (Found: C, 59·1; H, 9·0; N, 10·1. $C_7H_{13}O_2N$ requires C, 58·75; H, 9·1; N, 9·8%).

trans-2-2′-*Hydroxyethyl*cyclo*pentylamine*.—The foregoing oxime (6·5 g.) was dissolved in hot dry ethanol (140 c.c.) and treated with sodium (12 g.) added in portions during 30 min. The mixture was refluxed for 30 min., cooled, and acidified with 15% hydrochloric acid. After removal of ethanol under suction, the residual acid solution was washed with ether and basified, the liberated amine being recovered by ether-extraction. trans-2-2′-*Hydroxyethyl*cyclo*pentyl-amine* (3·4 g., 58%) distilled at 128—130°/13 mm. Crystallisation from light petroleum (b. p. 40—60°) gave prisms, m. p. 73—75° (Found: C, 65·2; H, 11·5; N, 10·7. $C_7H_{15}ON$ requires C, 65·1; H, 11·6; N, 10·9%). The *dibenzoyl derivative* (Schotten–Baumann) crystallised from light petroleum (b. p. 60—80°) in feathery needles, m. p. 109° (Found: C, 74·6; H, 6·7; N, 4·3. $C_{21}H_{23}O_3N$ requires C, 74·8; H, 6·8; N, 4·2%), and *picrolonate* from ethanol in orange prisms, m. p. 203—204° (Found: C, 51·8; H, 6·2. $C_{17}H_{23}O_6N_5$ requires C, 51·9; H, 5·9%).

trans-2-2′-*Bromoethyl*cyclo*pentylamine Hydrobromide*.—The foregoing hydroxy-amine (17 g.) was heated under reflux with 48% hydrobromic acid (800 c.c.) for 5 hr. The solution was evaporated to dryness under reduced pressure and the residue crystallised from ethyl acetate. The *bromo-amine hydrobromide* (20 g., 56%) was thus obtained as colourless plates, m. p. 148—149° (Found: C, 31·0; H, 5·5. Calc. for $C_7H_{15}NBr_2$: C, 30·8; H, 5·5%) (Prelog and Szpilfogel [2] record m. p. 140·5°). The *bromo-amine picrate*, prepared from the hydrobromide and aqueous picric acid, crystallised from water in yellow needles, m. p. 155° (Found: C, 36·8; H, 3·8. $C_{13}H_{17}O_7N_4Br$ requires C, 37·1; H, 4·0%).

trans-2 : 3-cyclo*Pentanopyrrolidine*.—A solution of the *trans*-bromo-amine hydrobromide (3·1 g.) in water (100 c.c.) was added during 5 hr. to a stirred solution of potassium hydroxide

(11 g.) in water (150 c.c.). Stirring was continued for a further 1 hr. and the mixture then extracted with ether. The ethereal extracts were shaken with dilute hydrochloric acid and the base was recovered from the acid extracts in the usual way. *trans*-2 : 3-*cyclo*Pentanopyrrolidine (0·75 g., 60%) was thus obtained as an oil, b. p. 173—176° (bath-temp.)/756 mm. A redistilled sample had b. p. (Siwoloboff) 167—168°/764 mm., n_D^{18} 1·4845, d^{18} 0·930, $[M]_R$ 34·1 (Calc. 33·7) (Prelog and Szpilfogel record b. p. 151—155°/731 mm., n_D^{21} 1·4867, d^{21} 0·9478). The base afforded the following derivatives: picrate, yellow rods (from water), m. p. 87—90° (varies with rate of heating), undepressed when mixed with a specimen, m. p. 87—90°, kindly provided by Professor Prelog (Found: C, 45·6; H, 4·4; N, 16·8. Calc. for $C_{13}H_{16}O_7N_4$: C, 45·9; H, 4·7; N, 16·5%); orange-yellow picrolonate (from ethanol), m. p. 239—240° (Found: N, 18·5. Calc. for $C_{17}H_{21}O_5N_5$: N, 18·7%); 3 : 5-*dinitrobenzoate* needles (from ethyl acetate), m. p. 157° (Found: C, 52·1; H, 5·1; N, 13·3. $C_{14}H_{17}O_6N_3$ requires C, 52·0; H, 5·3; N, 13·0%) (Prelog and Szpilfogel record the m. p. of picrate and picrolonate as 103—104° and 239·5° respectively).

trans-1-*Methyl*-2 : 3-cyclo*pentanopyrrolidine*.—*trans*-2 : 3-*cyclo*Pentanopyrrolidine (3·7 g.) was refluxed for 4 hr. with 40% aqueous formaldehyde (5 c.c.) and 90% formic acid (9 c.c.). Extraction of the basified solution with ether gave the tertiary amine (2·7 g., 59%), b. p. 51°/14 mm. The *picrate* crystallised from ethanol as yellow plates, m. p. 197—198° (Found: C, 47·8; H, 5·3; N, 15·7. $C_{14}H_{18}O_7N_4$ requires C, 47·5; H, 5·1; N, 15·8%); the *methiodide* crystallised from acetone–ethyl acetate in needles, m. p. 243° (decomp.) (Found: C, 40·8; H, 6·5; N, 5·1; I, 47·0. $C_9H_{18}NI$ requires C, 40·5; H, 6·7; N, 5·2; I, 47·5%).

Leuckardt Reaction with 2-2′-*Hydroxyethyl*cyclo*pentanone* (cf. Ingersoll [8]).—The hydroxy-ketone (13·9 g.) was added slowly to ammonium formate (35 g.), previously heated to 165° in an oil-bath. The temperature was then raised gradually to 180° and was kept there for 4 hr., an aqueous distillate being removed meanwhile. The product was then heated under reflux with aqueous sodium hydroxide (50 g. in 280 c.c.) for 3 hr. to hydrolyse the amides produced. The oily layer produced was worked-up by ether-extraction. Distillation gave the mixed amines (5·8 g., 41%), b. p. 135°/18 mm. The mixture partly solidified and the solid was removed. Crystallisation from light petroleum (b. p. 40—60°) gave colourless prisms of *trans*-2-2′-hydroxyethyl*cyclo*pentylamine (4·2 g.), m. p. and mixed m. p. 73—75°. The filtrate probably contained a mixture of *cis*- and *trans*-hydroxy-amines but separation of the *cis*-amine was not attempted.

2-*Dimethylaminomethyl*cyclo*pentanone* (cf. Mannich and Schaller [9]).—A mixture of *cyclo*pentanone (33·6 g.), dimethylamine hydrochloride (16·2 g.), methanol (10 c.c.), and 40% aqueous formaldehyde (15 g.) was heated under reflux on a steam-bath for 30 min. The cooled mixture was treated with water (50 c.c.) and extracted with ether to remove *cyclo*pentanone. The aqueous residue was cooled thoroughly in ice, basified, and extracted with ether. After removal of ether from the dried extracts, distillation afforded the Mannich base (8·6 g., 31%), b. p. 89—94°/18 mm. (Mannich and Schaller record b. p. 88—90°/15 mm. and do not quote a yield.)

2-2′-*Nitroethyl*cyclo*pentanone*.—A mixture of 2-dimethylaminomethyl*cyclo*pentanone (18·3 g.) and nitromethane (12·4 g.) was heated on a steam-bath and sodium methoxide (3·65 g.) in methanol (36·5 g.) was added gradually, with stirring. The semi-solid mass was then removed from the steam-bath, and methanol (24 c.c.) was added. The solution was set aside for an hour and then poured slowly into an ice-cold solution of acetic acid (16 g.) in water (150 c.c.). Extraction with ether gave the nitro-ketone (3·4 g., 17%), b. p. 135—138°/3 mm. The *semi-carbazone* crystallised from ethanol in colourless plates, m. p. 203° (decomp.) (Found: C, 45·1; H, 6·6; N, 26·0. $C_8H_{14}O_3N_4$ requires C, 44·9; H, 6·55; N, 26·2%).

Ethyl 2-*Hydroxyimino*cyclo*pentylacetate*.—A mixture of hydroxylamine hydrochloride (54 g.) and sodium hydrogen carbonate (61·5 g.) was added to a solution of ethyl 2-oxo*cyclo*pentyl-acetate (Linstead and Meade [10]) (90 g.) in moist ether (250 c.c.), and the mixture was heated under reflux for 12 hr. The ethereal solution was filtered, dried (Na_2SO_4), and evaporated. Distillation of the residue yielded the *hydroxyimino-ester* (90 g., 92%), b. p. 130—132°/0·5 mm., n_D^{21} 1·4813 (Found: C, 58·2; H, 8·2; N, 7·8. $C_9H_{15}O_3N$ requires C, 58·3; H, 8·2; N, 7·6%).

Hydrogenation of Ethyl 2-*Hydroxyimino*cyclo*pentylacetate over Raney Nickel*.—The hydroxy-imino-ester (30 g.), in dry ethanol (30 c.c.), was reduced over Raney nickel with hydrogen at an initial pressure of 70 atm. and at room temperature. After 4 hr., the mixture was filtered and

[8] Ingersoll, *J. Amer. Chem. Soc.*, 1936, **58**, 1808.
[9] Mannich and Schaller, *Arch. Pharm.*, 1938, **276**, 575.
[10] Linstead and Meade, *J.*, 1934, 935.

ethanol was removed by evaporation. The residue was separated by distillation into three fractions:

(i) *Ethyl* trans-2-*amino*cyclo*pentylacetate* (4·5 g.), b. p. 60—65°/0·5 mm., n_D^{19} 1·4616 (Found: C, 63·4; H, 9·8. $C_9H_{17}O_2N$ requires C, 63·2; H, 10·0%). The *benzoyl derivative* (Schotten–Baumann in sodium hydrogen carbonate solution) crystallised from benzene–light petroleum (b. p. 40—60°) in needles, m. p. 91—92° (Found: C, 70·0; H, 7·5. $C_{16}H_{21}O_3N$ requires C, 69·8; H, 7·7%). Reduction of the amino-ester (3 g.) in ether (70 c.c.) with lithium aluminium hydride (1 g.) gave *trans*-2-2′-hydroxyethyl*cyclo*pentylamine (1·2 g., 57%), m. p. and mixed m. p. 73—75° (picrolonate, m. p. and mixed m. p. 203—204°).

(ii) An oil (4·2 g.), b. p. 102—108°/0·5 mm., which crystallised on standing. Recrystallisation from light petroleum (b. p. 40—60°) gave cis-2 : 3-cyclo*pentanopyrrolid-5-one* as hygroscopic prisms, m. p. 51—53° (evacuated tube) (Found: C, 66·9; H, 8·9. $C_7H_{11}ON$ requires C, 67·2; H, 8·8%).

(iii) A basic oil (10·3 g.), b. p. 142—144°/0·5 mm. This was probably *di*-(2-*ethoxycarbonylmethyl*cyclo*pentyl*)*amine* (Found: C, 66·7; H, 9·7; N, 4·3. $C_{18}H_{31}O_4N$ requires C, 66·4; H, 9·6; N, 4·3%).

trans-2-*Amino*cyclo*pentylacetic Acid Hydrochloride*. Ethyl *trans*-2-amino*cyclo*pentylacetate (0·5 g.) was refluxed for 15 hr. with 7% hydrochloric acid (15 c.c.). The solution was evaporated to dryness under reduced pressure and the residue was crystallised from ethanol–ether. The *acid hydrochloride* (0·4 g., 76%) was thus obtained in prisms, m. p. 158—160° (Found: C, 47·0; H, 7·8. $C_7H_{14}O_2NCl$ requires C, 46·8; H, 7·8%).

cis-2-*Amino*cyclo*pentylacetic Acid Hydrochloride*.—*cis*-2 : 3-*cyclo*Pentanopyrrolid-5-one (0·5 g.) was refluxed for 3 hr. with 7% hydrochloric acid (10 c.c.). Hydrochloric acid (2 c.c.; 30%) was then added and the mixture was refluxed for a further 2 hr., and then evaporated to dryness. Crystallisation of the residue from ethanol–ether gave colourless prisms (0·6 g., 84%) of the cis-*acid hydrochloride*, m. p. 173—175° (decomp.) (Found: C, 46·9; H, 7·6%).

cis-2 : 3-cyclo*Pentanopyrrolidine*.—(*a*) *cis*-2 : 3-*cyclo*Pentanopyrrolid-5-one (2·6 g.) in ether (40 c.c.) was added dropwise to a solution of lithium aluminium hydride (1·5 g.) in ether (40 c.c.). After being heated under reflux for 2 hr., the mixture was cooled and diluted with moist ether to decompose excess of lithium aluminium hydride. The ethereal layer was separated and shaken with dilute hydrochloric acid. The acid solution was made alkaline and the base was extracted into ether. cis-2 : 3-cyclo*Pentanopyrrolidine* (1·4 g., 61%) was thus obtained as a colourless oil, b. p. 160—165° (bath temp.)/764 mm. A twice redistilled sample had b. p. (Siwoloboff) 161°/764 mm., n_D^{18} 1·4795, d_4^{18} 0·944, $[M]_R$ 33·4 (Calc., 33·7), and afforded the following derivatives: *picrate*, m. p. 111° (from benzene) (Found: C, 45·8; H, 4·8%); *picrolonate*, prisms (from ethanol), m. p. 204—205° (Found: C, 54·2; H, 5·8%); 3 : 5-*dinitrobenzoate*, plates, m. p. 201—203° (from ethyl acetate) (Found: C, 52·3; H, 5·4; N, 13·2%).

(*b*) 2-2′-Nitroethyl*cyclo*pentanone (2 g.) in methanol (65 c.c.) was hydrogenated over Raney nickel at room temperature and pressure. An absorption of hydrogen equivalent to that required for reduction of the nitro-group alone took place in 1—2 hr. The filtered solution was diluted with ethanol (65 c.c.), heated to boiling, and treated with sodium (11 g.), in portions during 30 min. The cooled solution was acidified and evaporated under reduced pressure to remove ethanol. Basification and ether extraction afforded *cis*-2 : 3-*cyclo*pentanopyrrolidine (0·2 g., 14%), b. p. 55—60°/17 mm., identified as the 3 : 5-dinitrobenzoate, m. p. and mixed m. p. 203° (Found: C, 52·4; H, 5·2; N, 13·0%).

THE UNIVERSITY, NOTTINGHAM.

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216. *The Raman Spectra of Mercuric Cyanide and the Tetracyanomercurate Ion.*

By L. A. Woodward and H. F. Owen.

Using a solution of mercuric cyanide in methyl alcohol, we have observed the complete Raman spectrum of the $Hg(CN)_2$ molecule and have determined the states of polarisation of the lines. The results confirm recent fundamental assignments based upon combination frequencies observed in infrared absorption. An aqueous solution of mercuric cyanide containing excess of sodium cyanide shows a Raman spectrum attributable to the $Hg(CN)_4^{2-}$ ion. The effect of complex-ion formation upon the bond-stretching force constants is discussed.

The object of this work was to investigate the changes of the stretching force constants of the Hg–C and C–N bonds produced by co-ordination of two cyanide ions with the $Hg(CN)_2$ molecule to form the $Hg(CN)_4^{2-}$ complex ion.

Raman Spectrum of the $Hg(CN)_2$ *Molecule.*—The linear symmetrical $Hg(CN)_2$ molecule (point group $D_{\infty h}$) must have seven distinct fundamental frequencies, of which three ($2\Sigma_g^+ + 1\Pi_g$) are permitted in the Raman effect but forbidden in infrared absorption and the remaining four ($2\Sigma_u + 2\Pi_u$) are forbidden in the Raman effect but permitted in the infrared. Of the three Raman-permitted fundamentals, two (class Σ_g^+, frequencies ν_1 and ν_2) should appear as polarised lines and the other (class Π_g, frequency ν_5) as a depolarised line.

The Raman spectrum of $Hg(CN)_2$ has been previously investigated both in the solid state [1] and in solutions in water [2] and methyl alcohol,[3,4] where the degree of ionic dissociation is very low. All previous workers agree in finding a strong line at about $\Delta\nu = 2200$ cm.$^{-1}$, which must obviously be assigned to the totally symmetrical mode involving principally C–N stretching, *i.e.*, to ν_1. Some previous workers also report a second, weaker line at about 270 cm.$^{-1}$, which they attribute (not unnaturally) to the symmetrical mode involving principally Hg–C stretching, *i.e.*, to ν_2. Only François,[4] using a solution of mercuric cyanide in methyl alcohol, reports all the three lines expected for the $Hg(CN)_2$ molecule on the basis of the selection rules. His frequencies are 2204, 404, and 273 cm.$^{-1}$. Since 2204 cm.$^{-1}$ must certainly be assigned to ν_1, only one of the two remaining frequencies should be polarised. The only work on polarisation of the lines appears to be that of François [4] and he reports the anomalous finding that 404 and 273 cm.$^{-1}$ are both polarised.

Recently Jones [5] studied the infrared absorption of solid mercuric cyanide. Both ν_2 and ν_5 are forbidden in the infrared region as fundamentals, but Jones deduced from observed combinations that ν_2 must lie at 415 ± 5 cm.$^{-1}$ and ν_5 at 276 ± 5 cm.$^{-1}$. That the observed Raman frequency near 270 cm.$^{-1}$ should be ν_5 rather than ν_2 is contrary to all previous assignments, though admittedly these had been made without satisfactory evidence as to polarisation.

We have photographed the complete three-line Raman spectrum of the $Hg(CN)_2$ molecule in approximately 1·2M-mercuric cyanide in methyl alcohol. Aqueous solutions were also studied, but owing to the relatively low solubility (about 0·4M) and the spectra being impaired by a troublesome continuum, it was not possible to obtain all three Raman frequencies with certainty.

Table 1 gives the frequencies for the methyl alcoholic solution, the states of polarisation as determined with polarised incident light, and the estimated intensities. The polarisation evidence conclusively shows that 274 cm.$^{-1}$ is to be assigned to ν_5 and 412 cm.$^{-1}$ to ν_2. This is in complete accord with Jones's conclusions.[5]

[1] Krishnamurti, *Indian J. Phys.*, 1930, **5**, 651.
[2] Woodward, *Physikal. Z.*, 1930, **17**, 792; Braun and Engelbrecht, *Z. phys. Chem.*, 1931, **11**, 409.
[3] Petrikaln and Hochberg, *ibid.*, 1930, **8**, 440.
[4] François, *Compt. rend.*, 1939, **208**, 1002.
[5] Jones, *J. Chem. Phys.*, 1957, **27**, 665.

Raman Spectrum of the $Hg(CN)_4^{2-}$ *Ion.*—In aqueous solution and in the presence of excess of CN^- ions mercuric cyanide is almost completely converted into the tetracyanomercurate ion: $Hg(CN)_2 + 2CN^- = Hg(CN)_4^{2-}$. The Raman spectrum is expected to show (in addition to the single frequency, *ca.* 2080 cm.$^{-1}$, of the excess of cyanide ions) a number of lines due to the complex ion. Since the ion is tetrahedral (point group T_d) only

TABLE 1. *Raman spectrum of* $Hg(CN)_2$.

$\Delta\nu$ (cm.$^{-1}$)	Polarisation	Intensity	Assignment
274	Depolarised	weak	ν_5 (Π_g)
412	Polarised	weak	ν_2 (Σ_g^+)
2189	Polarised	strong	ν_1 (Σ_g^+)

two of these lines will be polarised, namely, those corresponding to the totally symmetric modes which involve mainly C–N stretching (frequency ν_1) and Hg–C stretching (frequency ν_2) respectively. Moreover owing to the spherical symmetry of the polarisability ellipsoid of the $Hg(CN)_4^{2-}$ ion these two lines will be completely polarised ($\rho = 0$) and so will be clearly distinguishable from all the others (for which $\rho = \frac{6}{7}$).

Again the aqueous solutions investigated were found to give Raman spectra with a troublesome continuum, which doubtless masked weaker lines. Nevertheless by suitable choice of concentration and exposure time it was found possible to observe three Raman frequencies: 2148 (strong), 342 (very weak), and 200 cm.$^{-1}$ (very weak). In addition the spectrum showed the line due to CN^-, the measured frequency of which was 2082 cm.$^{-1}$.

The line at 2148 and the line at 342 cm.$^{-1}$ are both polarised. This conclusively determines their assignments as ν_1 and ν_2 respectively.

Stretching Force Constants.—For $Hg(CN)_2$, using a simple valency force field, we obtain from the frequencies $\nu_1 = 2189$ and $\nu_2 = 412$ cm.$^{-1}$ (see Table 1) the values $k_{C-N} = 17{\cdot}3 \times 10^5$ and $k_{Hg-C} = 2{\cdot}74 \times 10^5$ dynes/cm. for the stretching force constants of the C–N and Hg–C bonds respectively. Using a potential including interaction terms, Jones [5] arrived at the values $k_{C-N} = 17{\cdot}6 \times 10^5$ and $k_{Hg-C} = 2{\cdot}61 \times 10^{-5}$. The simple valency force field is evidently quite a good approximation.

For $Hg(CN)_4^{2-}$, likewise using a simple valency force field, we obtain from the frequencies $\nu_1 = 2148$ and $\nu_2 = 342$ cm.$^{-1}$ the values $k_{C-N} = 17{\cdot}0 \times 10^5$ and $k_{Hg-C} = 1{\cdot}85 \times 10^5$.

The $Hg(CN)_4^{2-}$ ion is formed from the $Hg(CN)_2$ molecule by the attachment of two CN^- ions, each of which forms a co-ordinate link with the mercury atom by the donation of a pair of electrons from its carbon atom. There is no reason to doubt that in the ion Hg is joined to the four C atoms by single bonds, for this completes the rare-gas valency octet of the mercury atom. In the $Hg(CN)_2$ molecule it is possible that the Hg–C bonds may have a small amount of double-bond character from π-bonding, as in $N^+{=}C{\rightleftarrows}Hg^-{-}C{\equiv}N$. Nevertheless in the formation of the ion from the molecule there is doubtless an increase in the number of electrons in the valency shell of the mercury atom, and this has two simultaneous and related consequences: (*a*) the screening of the Hg nucleus is increased and the effective value of its positive charge is diminished and (*b*) the linear arrangement of the two Hg–C bonds in the $Hg(CN)_2$ molecule gives place to the regular tetrahedral arrangement of the four bonds of the complex ion. Insofar as it is permissible to consider (*a*) and (*b*) separately, the effect of (*a*) will be to loosen the Hg–C bonds and so to lower the force constant k_{Hg-C}. The effect of (*b*) is difficult to assess, but is not likely to be large: in view of the marked stability of tetrahedral bond arrangements, (*b*) might possibly tend to cause some increase of k_{Hg-C}, but (as pointed out above) a small lowering of bond order may be involved. In fact, as we have seen, the observed overall effect is a very marked fall in k_{Hg-C}, so that probably the principal influence is the reduction of the effective positive charge of the Hg nucleus by the accession of electrons from the co-ordination of the CN^- ions.

A similar phenomenon is observed [6] in the formation of ions of the type HgX_4^{2-} from the corresponding mercuric halide molecules HgX_2, where X is Cl, Br, or I (see Table 2). The frequencies of the HgX_2 molecules were all observed for solutions in non-dissociating solvents; those of the complex ions HgX_4^{2-} for aqueous solutions containing an excess of X^- ions. Table 2 includes also the present results. The ratio of k_{Hg-C} in the $Hg(CN)_2$ molecule to that in the $Hg(CN)_4^{2-}$ ion is remarkably close to the corresponding ratios for the halides.

TABLE 2. *Stretching force constants of* Hg–X *bonds.*

Species	Symmetrical stretching frequencies (cm.$^{-1}$)	$10^{-5}k_{Hg-X}$ (dynes/cm.)	$\frac{k_{Hg-X} \text{ in } HgX_2}{k_{Hg-X} \text{ in } HgX_4^{2-}}$
$HgCl_2$	325	2·21	1·46
$HgCl_4^{2-}$	269	1·51	
$HgBr_2$	205	1·98	1·52
$HgBr_4^{2-}$	166	1·30	
HgI_2	150	1·68	1·51
HgI_4^{2-}	122	1·11	
$Hg(CN)_2$	2189 & 412	2·74	1·48
$Hg(CN)_4^{2-}$	2148 & 342	1·85	

The case of $HgCl_2$ and $HgCl_4^{2-}$ is specially interesting. We have supposed that the drop of k_{Hg-Cl} on passing from the molecule to the complex ion is due mainly to the reduction of the effective positive charge of the central nucleus. The effect of increasing the actual charge of the central nucleus (without altering the tetrahedral structure) can be seen by considering the isoelectronic molecule $PbCl_4$. In this the atomic number Z of the central atom has risen by two units without any alteration of the number of electrons present. The value of ν_1 for $PbCl_4$ is [7] 327 cm.$^{-1}$, from which we obtain the bond-stretching force constant $2{\cdot}23 \times 10^5$ dynes/cm. This is not only higher than in the $HgCl_4^{2-}$ ion, but is also higher than in the $HgCl_2$ molecule. Possible effects of change of bond orientation and bond order being ignored, it appears that (as expected) the reduction of the effective positive charge of the Hg nucleus caused by the donation of two pairs of electrons in the co-ordination of two Cl^- ions is considerably less than the increase caused by a rise of 2 in Z.

As regards the stretching force constant of the C–N bond, the calculated value for the $Hg(CN)_4^{2-}$ ion is slightly lower than that for the $Hg(CN)_2$ molecule. In view of the approximate force field used, however, it is doubtful whether the small difference (17·0 compared with 17·3) is significant. It is not unreasonable to expect that a small drop of k_{C-N} might accompany the drop of k_{Hg-C}; for the latter has been explained above as due to a diminution of the attraction of the Hg nucleus for the bonding electrons, and this will cause a corresponding accession of electronic charge by the carbon atoms with consequent increased screening of the carbon nuclei and loosening of the C–N bonds.

The $Hg(CN)_2$ molecule itself can be thought of as formed by the co-ordination of two cyanide ions with a mercuric ion: $Hg^{2+} + 2CN^- = NC{\rightarrow}Hg{\leftarrow}CN$. The frequency ν_1 of the mainly C–N stretching vibration of the $Hg(CN)_2$ molecule is higher than the frequency of the CN^- ion, but this fact does not in itself mean that k_{C-N} is larger in the molecule than in the ion. Even if k_{C-N} were the same in both species, the mechanical coupling in the molecule must give rise to a frequency difference in the observed direction. In the case under consideration, however, calculation shows that k_{C-N} in the CN^- ion is $16{\cdot}5 \times 10^5$, so that there is a small but definite increase associated with the formation of the $Hg(CN)_2$ molecule. This is as expected on the view (cf. above) that the donation of electron pairs to the Hg^{2+} ion by the C atoms of the CN^- ions must reduce the screening of the C nuclei, thus increasing their effective positive charge and tightening the C–N bonds.

Experimental.—Each solution was passed through a fine sintered glass filter into the Raman vessel. The spectra were excited by a Toronto-type mercury-arc lamp, the principal exciting

[6] Rolfe, Sheppard, and Woodward, *Trans. Faraday Soc.*, 1954, **50**, 1275.
[7] Neu and Gwinn, *J. Amer. Chem. Soc.*, 1948, **70**, 3463.

line being 4358 Å. Primary lines of lower wavelengths were effectively suppressed by the use of a filter of *m*-dinitrobenzene in benzene. The spectrograph was a Hilger E 612 instrument (two prisms and *f*/5·7 camera) giving a reciprocal dispersion of about 18 Å per mm. in the region studied. For each solution a wide range of exposure times was explored in order to find the best. The states of polarisation of the Raman lines were determined qualitatively by taking successive photographs with suitably oriented polaroid cylinders surrounding the Raman tube. Kodak special scientific plates, emulsion type Oa and sensitivity G, were used throughout. Frequencies were measured in the usual manner with an iron-arc spectrum as standard. For strong lines the limits of error of the measured $\Delta\nu$ values are estimated at ± 2 cm.$^{-1}$, but for very weak lines the errors may be larger.

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INORGANIC CHEMISTRY LABORATORY,
SOUTH PARKS ROAD, OXFORD.

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217. *Urea and Related Compounds. Part VI.** sym-*Diaryldithioformamidines.*

By FREDERICK KURZER and PHYLLIS M. SANDERSON.

sym-Diaryldithioformamidines are obtained by oxidising aromatic thioureas with bromine and are isolated in the form of suitable salts. Hydrolysis of *sym*-diaryldithioformamidines in alkaline media yields, according to the conditions, sulphur, arylthioureas, *sym*-diarylguanidines, arylcyanamides, and 2 : 4-diaryl-3 : 5-di-imino-1 : 2 : 4-thiadiazolidines.

An improved technique of preparing 2 : 4-diaryl-3 : 5-di-imino-1 : 2 : 4-thiadiazolidines by oxidising aromatic thioureas with hydrogen peroxide is described.

WHEREAS thiourea and its alkyl derivatives are readily oxidised to the corresponding disulphides (I; R = H or Alk), the existence of *sym*-diaryldithioformamidines (I; R = Ar) has long been doubted. Oxidation of arylthioureas, expected to furnish the desired disulphides (I; R = Ar), invariably gave heterocyclic products. The relevant literature has been summarised briefly before.[1]

We have recently[1] reported the conversion of aromatic thioureas into dithioformamidines, but our work was restricted to *ortho*-substituted arylthioureas: this choice of starting material was intended to exclude the possibility of the ring closure to benzothiazoles,[2,3] which, according to the literature, is the prevalent reaction under these conditions. It was desirable to examine the applicability of this synthesis to arylthioureas which lacked *ortho*-substituents; *sym*-diaryldithioformamidines were expected to prove useful in the study of the hydrolysis of dithioformamidine and of the course of the oxidation of arylthioureas to 2 : 4-diaryl-3 : 5-di-imino-1 : 2 : 4-thiadiazolidines.†

Experiments have shown that blocking the *ortho*-positions of the aromatic nuclei of arylthioureas is not essential to prevent cyclisation and that, under proper conditions, *sym*-diaryldithioformamidines (I; R = Ar) appear to be generally obtainable. Arylthioureas, suspended in inert organic solvents, reacted rapidly with the calculated quantity of bromine at room temperature and gave excellent yields of the dithioformamidines (I; R = Ar), which were isolated as hydrobromides. The oxidation was promoted by the

* Part V, *J.*, 1958, 1571.

† Following accepted practice, we continue to represent, with the usual reservations (cf. Part IV [1]), so-called Hector's bases as 2 : 4-diaryl-3 : 5-di-imino-1 : 2 : 4-thiadiazolidines.

[1] Kurzer and Sanderson, *J.*, 1957, 4461.
[2] Hugershoff, *Ber.*, 1901, **34**, 3130; 1903, **36**, 3121, 3134; 1906, **39**, 1014.
[3] Sahasrabudhey and Krall, *J. Indian Chem. Soc.*, 1944, **21**, 17.

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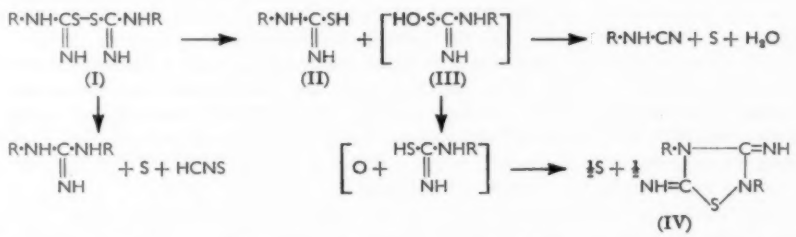
presence of small quantities of water; under anhydrous conditions, the rate of bromine uptake was much reduced, and reaction stopped completely after 60—70% of the halogen had been added. Since dithioformamidines (I) are unobtainable as free bases, they were further characterised as picrates and picrolonates. All salts, though reasonably stable as the dry solid, decomposed rapidly in contact with solvents, including non-polar ones, and could not, therefore be purified by crystallisation. A technique was devised, however, which afforded excellent yields of analytically pure salts in one stage; with careful attention to correct conditions (cf. Experimental) results were consistently reproducible. It is known [4] that salts of the parent compound (I; R = H) also tend to decompose on attempted crystallisation and are best prepared under conditions that afford pure specimens in one operation. Fichter *et al.*, during a study of the electrolytic oxidation of organic sulphur compounds,[5] converted thioureas into dithioformamidines; [6] although they obviously succeeded in preparing *sym*-diphenyldithioformamidine hydrochloride, the only aromatic example studied, their attempts to isolate the salt resulted in its partial decomposition.

As expected, bis-(*N*-alkyl-*N*-aryl)dithioformamidines are also obtained by this reaction. *N*-Ethyl-*N*-phenylthiourea, for example, was oxidised more smoothly than any of the arylthioureas, the reaction being completed rapidly even in the absence of water; in contrast, dialkylthioureas are preferably oxidised in aqueous media.[1,7] Bis-(*N*-ethyl-*N*-phenyl)dithioformamidine hydrobromide thus obtained was more stable than the *sym*-diaryl derivatives (I; R = Ar), being crystallisable from suitable solvents in the cold. On the other hand, attempts to prepare dithioformamidines from *sym*- and *asym*-diphenylthioureas were unsuccessful. Although both thioureas absorbed the correct amount of halogen the solutions thus obtained gave an uncrystallisable yellow oil from the *sym*- and solids of variable composition and m. p. from the *asym*-material. Both substances dissolved in mineral acids and deposited sulphur on basification, and no doubt consisted substantially of the desired products.



The course of the reaction between arylthioureas and halogens in non-polar solvents thus depends clearly on the conditions: the use of equimolar quantities or excess of bromine at higher temperatures provides an excellent route to 2-aminobenzothiazoles (" Hugershoff's synthesis "),[2,3,8] but half-molar proportions of the oxidising agent under mild conditions afford dithioformamidines.

Dithioformamidines exist only as the salts, solutions of which deposit sulphur immediately when attempts are made to liberate the free bases. Precise information is, however, not available on the decomposition of these disulphides in alkaline media. Claus,[9] hydrolysing dithioformamidine hydrobromide in boiling water, obtained sulphur, and impure thiourea containing a sulphur-free by-product, the latter components being

[4] McGowan, *J.*, 1886, **49**, 190; *J. prakt. Chem.*, 1886, **33**, 188.
[5] Fichter and Sjöstedt, *Ber.*, 1910, **43**, 3422; Fichter and Wenk, *ibid.*, 1912, **45**, 1373.
[6] Fichter and Braun, *Ber.*, 1914, **47**, 1528.
[7] Sahasrabudhey and Singh, *J. Indian Chem. Soc.*, 1952, **29**, 636.
[8] Sprague and Land, in Elderfield (Ed.), " Heterocyclic Compounds," Wiley, New York, 1957, Vol. 5, p. 581.
[9] Claus, *Annalen*, 1875, **179**, 135, 140.

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only incompletely separable from one another; he represented the decomposition by (1). Later workers,[4, 10, 11] observing the deposition of sulphur, interpreted the alkaline hydrolysis in the same way without further experimental evidence. Analogous assumptions were made for the decomposition of *sym*-diphenyldithioformamidine hydrochloride in contact with water.[6]

$$C_2H_6N_4S_2,2HBr \longrightarrow 2HBr + S + CS(NH_2)_2 + NH_2{\cdot}CN \quad . \quad . \quad . \quad . \quad . \quad (I)$$

Diaryldithioformamidines appeared to be particularly suitable for hydrolysis studies because of the ease with which products can be isolated and characterised. Results show that the alkaline hydrolysis of *sym*-diaryldithioformamidines (I) cannot be represented by a simple equation such as (1), but appears to involve simultaneous and consecutive changes. Alkali rapidly decomposed *sym*-diphenyldithioformamidine into sulphur, phenylthiourea, phenylcyanamide, and *sym*-diphenylguanidine, while the action of ammonia afforded sulphur, phenylthiourea, and, unexpectedly, 3 : 5-di-imino-2 : 4-diphenyl-1 : 2 : 4-thiadiazolidine. Although the results do not establish the route by which the products are formed, it is suggested that in both cases, the first stage may be the hydrolytic cleavage of the disulphide link of (I) to form the arylthiourea (II) and an intermediate highly labile sulphenic acid (III). The existence of an analogous sulphinic acid, $NH_2{\cdot}C(:NH){\cdot}SO_2H$, obtainable from thiourea or dithioformamidine salts on oxidation, is well established.[12, 13] Decomposition of the hypothetical intermediate (III) might proceed, in the former hydrolysis, to yield cyanamide and sulphur, but may take place, in ammoniacal medium, with preliminary elimination of oxygen, which thus becomes available for converting half the total arylthiourea formed into the thiadiazolidine (IV). The yields of products obtained in the reaction with ammonia are in agreement with this interpretation. The formation of " Hector's bases " (IV), the existence of which appears to be confined to the aromatic series,[14] presumably has no parallel in the hydrolysis of dithioformamidine itself and its alkyl derivatives, but suggests that oxidative changes may occur during their hydrolysis. *sym*-Diarylguanidine, isolated in relatively low yield, may arise more directly from (I), with elimination of sulphur and thiocyanic acid, which is always present in the hydrolysate. Further work in this connexion is in progress.

Finally, we report an improved procedure for preparing 2 : 4-diaryl-3 : 5-di-imino-1 : 2 : 4-thiadiazolidines (IV) from arylthioureas by oxidation. On decreasing the proportion of water present in the reaction mixture, by using 30% (instead of the usual 6%) hydrogen peroxide, and absolute ethanol as solvent, the heterocyclic compounds were obtained in significantly increased yields. Thus, thiadiazolidines (IV) derived from phenyl- and *p*-tolyl-thiourea, which we obtained by Hector's method [15] in 50 and 30% yield, were formed in 75—80% and 50% yield, respectively, by the improved technique. It is probable that the modified conditions prevent loss of reactant by hydrolytic side-reactions: the oxidation of phenylthiourea by 6% hydrogen peroxide in aqueous ethanol, for example, gave up to 15% of *sym*-diphenylguanidine as by-product (see also Part IV [1]).

Experimental

The solvent used for preparing M-bromine was chloroform, unless otherwise stated.

Bromide in *sym*-diphenyl- and bis-(*N*-ethyl-*N*-phenyl)-dithioformamidine dihydrobromides was estimated by Volhard's method, including the use of nitrobenzene (cf. Part IV [1]). The other dithioformamidine hydrobromides precipitated silver sulphide rapidly from 0·1N-silver nitrate, and bromide was estimated gravimetrically in these cases.

[10] Storch, *Monatsh.*, 1890, **11**, 458.
[11] Sahasrabudhey, *J. Indian Chem. Soc.*, 1950, **27**, 433.
[12] Barnett, *J.*, 1910, **97**, 63.
[13] Boeseken, *Proc. Akad. Sci. Amsterdam*, 1936, **39**, 717; *Rec. Trav. chim.*, 1936, **55**, 1044; 1948, **67**, 603.
[14] Hector, *J. prakt. Chem.*, 1891, **44**, 492, and own unpublished observations.
[15] Hector, *Ber.*, 1889, **22**, 1177; 1890, **23**, 357.

Contact of wet dithioformamidine salts with metal spatulas must be avoided to prevent local decomposition.

sym-*Diphenyldithioformamidine.*—(*a*) A suspension of finely ground phenylthiourea (6·08 g., 0·04 mole) in chloroform (100 ml.), to which water (6 ml.) was added, was treated with M-bromine (20 ml., 0·02 mole) with shaking and external cooling (ice–water) during 8—10 min. The product was filtered off, washed successively with much chloroform and light petroleum, ground in a mortar with more chloroform, collected, and dried at room temperature. The resulting white granular powder (8·0—9·2 g., 80—92%) was sym-*diphenyldithioformamidine dihydrobromide dihydrate*, m. p. 96—100° (decomp., frothing at 110—115°) [Found: C, 33·45; H, 4·0; N, 11·6; S, 13·0; Br (gravimetrically), 32·2; Br (volumetrically), 32·1. $C_{14}H_{14}N_4S_2,2HBr,2H_2O$ requires C, 33·6; H, 4·0; N, 11·2; S, 12·8; Br, 32·0%]. The product dissolved in 3N-hydrochloric or sulphuric acid when slightly warmed, but the solutions deposited colloidal sulphur when boiled, or in the cold on being basified. The salt was almost insoluble in hot benzene, light petroleum, or ether. It dissolved in warm ethanol or cold methanol; the former solution gave colloidal sulphur rapidly, the latter more slowly.

(*b*) Specimens of phenylthiourea consisting of large prisms, in spite of being finely ground, tended to absorb bromine erratically and form bright orange specks that were only slowly decolorised. In such cases, satisfactory results were obtained by continuously grinding the reactant (0·04 mole) with chloroform (15—20 ml.)–water (2 ml.) in a mortar and introducing 0·2M-bromine (0·02 mole) during 10—15 min. The yield of product, isolated as before, averaged 75% of the theoretical.

Addition of water to the reaction mixture in this and the subsequent preparations increases the rate and completeness of oxidation (see p. 1058), and appears to prevent local production of perbromide.

The absence of Hector's base [1] in the *sym*-diphenyldithioformamidine salt was demonstrated by extracting a sample (4 g.) with 3N-hydrochloric acid (10 ml.): the filtered extract when basified gave a precipitate that was not soluble in acid.

sym-*Di*-p-*tolyldithioformamidine.*—In a mortar, a suspension of finely powdered *p*-tolylthiourea (3·32 g., 0·02 mole) in chloroform (25 ml.)–water (2 ml.) was treated, with continuous grinding during 20—30 min., with M-bromine (10 ml.; 0·01 mole), more chloroform being added to make up for losses due to evaporation. The resulting white creamy precipitate was collected and washed with much chloroform, and the compact filter-cake ground with more chloroform and again collected. The white sym-*di*-p-*tolyldithioformamidine dihydrobromide* (3·9—4·4 g., 80—90%) had m. p. 95—98° (decomp., after sintering at 85°) (Found: C, 38·6; H, 4·1; N, 11·3; S, 13·0. $C_{16}H_{18}N_4S_2,2HBr$ requires C, 39·0; H, 4·1; N, 11·4; S, 13·0%). The product dissolved rapidly in cold methanol (absence of the sparingly soluble *p*-tolylthiourea); the solution slowly depositing colloidal sulphur.

o-Tolylthiourea (0·20 mole) absorbed the correct quantity of bromine on treatment by the above method, but gave clear chloroform solutions from which the soluble dithioformamidine salt could not be isolated without extensive decomposition.

Di-p-*chlorophenyldithioformamidine.*—*p*-Chlorophenylthiourea (1·87 g., 0·01 mole) was oxidised with bromine (0·005 mole) as described for the *p*-tolyl analogue. The precipitated salt was washed, re-ground with much chloroform, and dried, giving *di*-p-*chlorophenyldithioformamidine dihydrobromide* (2·25 g., 85%), m. p. 145—146° (decomp.; discolouring at 140°) (Found: C, 31·9; H, 2·9; N, 10·2; S, 11·7. $C_{14}H_{12}N_4S_2Cl_2,2HBr$ requires C, 31·5; H, 2·6; N, 10·5; S, 12·0%).

Bis-(N-*ethyl*-N-*phenyl*)*dithioformamidine.*—(i) *N*-Ethyl-*N*-phenylthiourea was prepared by a modification of Gerhardt's method [16] as follows: In a porcelain dish, *N*-ethylanilinium chloride (63 g., 0·4 mole), dissolved in warm water (300 ml.) containing concentrated hydrochloric acid (6 ml.), and ammonium thiocyanate (38 g., 0·5 mole) were kept at 100° during 1 hr. The liquid was set aside at room temperature during 2 hr., then slowly evaporated, and the residue heated on the steam-bath (total, 8—10 hr.). The residue was ground with water (3 × 100 ml.), and the product collected and crystallised from ethanol (2 ml. per g.). It formed massive needles, m. p. 111—112° (lit.[16] 113°) (yield, including material from the mother liquors, 48—56%).

(ii) A solution of *N*-ethyl-*N*-phenylthiourea (1·80 g., 0·01 mole) in cold chloroform (10 ml.) rapidly decolorised 1M-bromine (5 ml., 0·005 mole). The resulting liquid was diluted with ether to incipient precipitation; it deposited crystals, which were collected at 0°, washed with

[16] Gerhardt, *Ber.*, 1884, **17**, 2094.

cold chloroform, and air-dried [m. p. 158—160° (decomp.); 2·2—2·35 g., 85—90%]. Two crystallisations, by dissolution in the minimum of cold methanol, dilution with an equal volume of acetone, and dilution with ether to incipient turbidity (recovery 50—60%), gave lustrous prismatic *bis*-(*N-ethyl-N-phenyl*)*dithioformamidine dihydrobromide*, m. p. 162—163° (decomp.) (Found: C, 41·7; H, 4·6; N, 10·6; S, 12·1; Br, 30·9. $C_{18}H_{22}N_4S_2,2HBr$ requires C, 41·6; H, 4·6; N, 10·8; S, 12·3; Br, 30·7%). The salt was highly soluble in cold methanol, soluble in hot chloroform (slight decomp.), and sparingly soluble in water and cold chloroform.

Picrates.—These were prepared in 50—60% yield as follows: The finely powdered hydrobromide (0·001 mole) was dissolved in successive small quantities of the cold solvent [for (i): 40 ml. of 0·3N-hydrochloric acid; for (ii)—(iv): minimum (10—15 ml.) of methanol] and filtered into stirred cold 0·05N-aqueous picric acid (40—50 ml.; 0·002—0·0025 mole). The coagulated yellow powdery precipitate was collected, washed with 0·1N-hydrochloric acid, and air-dried.

Picrolonates.—These were similarly obtained in 60—90% yield as follows: A solution of the finely powdered hydrobromide (0·0004 mole) in cold hydrochloric acid [for (i): 30 ml. of 0·3N; (ii) 10 ml. of 1·5N; (iii) 25 ml. of 1·5N; (iv) 30 ml. of 1·5N + 30 ml. of methanol] was filtered into a stirred solution of picrolonic acid (0·26 g., 0·001 mole) in 0·3N-hydrochloric acid (60—80 ml.). The powdery yellow precipitate was collected, washed with very dilute hydrochloric acid, and dried at room temperature.

Specimens of *picrates* and *picrolonates* so obtained were analytically pure (cf. Table) but

				Found (%)		Required (%)	
R	R′	Formula	M. p.*	C	H	C	H
		Picrates $[RR'N{\cdot}C(:NH){\cdot}S]_2,\ 2C_6H_3O_7N_3$					
(i) Ph	H	$C_{26}H_{20}O_{14}N_{10}S_2$	105—106°	41·3	2·6	41·05	2·6
(ii) Ph	Et	$C_{30}H_{28}O_{14}N_{10}S_2$	99—100°	44·2	3·4	44·1	3·4
(iii) *p*-$CH_3{\cdot}C_6H_4$	H	$C_{28}H_{24}O_{14}N_{10}S_2$	68—71°	43·0	3·0	42·6	3·0
(iv) *p*-ClC_6H_4	H	$C_{26}H_{18}O_{14}N_{10}S_2Cl_2$	125—126°	38·1	2·6	37·6	2·2
		Picrolonates $[RR'N{\cdot}C(:NH){\cdot}S]_2,2C_{10}H_8O_5N_4$					
(i) Ph	H	$C_{34}H_{30}O_{10}N_{12}S_2,2H_2O$	130—132°	47·2	3·7	47·1	3·9
(ii) Ph	Et	$C_{38}H_{38}O_{10}N_{12}S_2$	103—105°	51·2	3·9	51·5	4·3
(iii) *p*-$CH_3{\cdot}C_6H_4$	H	$C_{36}H_{34}O_{10}N_{12}S_2,2H_2O$	149—150°	48·6	3·9	48·3	4·25
(iv) *p*-ClC_6H_4	H	$C_{34}H_{28}O_{10}N_{12}S_2Cl_2$	132—133°	45·4	2·8	45·4	3·1

* All products melted with decomposition.

decomposed on attempted crystallisation from the usual solvents. Because of the rapidity with which some of the *NN′*-diaryldithioformamidine hydrobromides decompose in solution, the procedure is not suitable for preparing picrates or picrolonates on a considerably larger scale.

sym-*Diphenyldithioformamidine.*—(a) ***Reaction with ammonia.*** Freshly prepared, finely powdered *sym*-diphenyldithioformamidine dihydrobromide dihydrate (10 g., 0·02 mole) was dissolved in boiling methanol (20 ml.), treated with aqueous ammonia (*d* 0·88; 6 ml., 0·12 mole), and the liquid swirled and boiled during 5 min. Colloidal sulphur, followed by a white crystalline solid, appeared in suspension; the whole was allowed to cool to room temperature and diluted with water (30 ml.), and the solids were collected at 0° and washed with a little water (ammoniacal filtrate: F) (5·26—5·65 g.). (i) The substance was exhaustively extracted with cold 3N-hydrochloric acid (2 × 10, 2 × 8 ml. successively), the undissolved solid collected (filtrate: E), and the dried product (2·9—3·2 g.) crystallised from methanol–water (1 : 3): the insoluble residue, removed by vacuum filtration, was sulphur (0·24—0·3 g.; 75—94%); the filtrates deposited phenylthiourea, m. p. and mixed m. p. 152—153° (2·6—2·8 g., 85—92%, including material from the mother-liquors). Filtrates E were basified with 3N-sodium hydroxide, and the precipitate was collected at 0°, washed with water, dried (1·95—2·4 g.) and crystallised from acetone–methanol (1 : 1), affording 3 : 5-di-imino-2 : 4-diphenyl-1 : 2 : 4-thiadiazolidine, m. p. and mixed m. p. 186—187° (deep red melt, decomp.) (total, including material from the mother-liquors, 1·5 g., 56%).

(ii) Alternatively, the crude base from E was treated, in pyridine, with toluene-*p*-sulphonyl chloride; the product, crystallised from acetone–ethanol, was the toluene-*p*-sulphonyl derivative of 3 : 5-di-imino-2 : 4-diphenyl-1 : 2 : 4-thiadiazolidine, m. p. and mixed m. p. 230—232° (2·70 g., 64%).

XUM

The ammoniacal filtrate F, having evaporated spontaneously at room temperature to quarter volume, gave a little solid (0·25 g.) consisting substantially of phenylthiourea.

Reaction using N- or 2N-aqueous ammonia (30 ml.) was more difficult, the reactant being converted, without completely dissolving, into a lumpy mass. This was fractionated into the same products as above, though in lower yields.

(b) *Alkaline hydrolysis.* Finely powdered dihydrobromide (5·0 g., 0·01 mole) was quickly dissolved in warm methanol (10 ml.) and treated with 3N-aqueous sodium hydroxide (10 ml., 0·03 mole). The mixture was boiled gently, with frequent swirling, during 5 min., set aside at room temperature, and the white precipitate (2·05—2·15 g.) collected at 0° (alkaline filtrate: G). It was extracted with cold 3N-hydrochloric acid (3 × 5 ml.), and the undissolved residue R collected and rinsed with water (filtrate: H). Product R (m. p. 147—149°) was crystallised from boiling methanol–water (1 : 3; 10 ml. per g.), a little undissolved sulphur (0·2—0·25 g.) being removed, and gave phenylthiourea, m. p. and mixed m. p. 152—153° (total, 1·05—1·22 g., corresponding to a 35—40% conversion of the reactant into thiourea). Filtrate H was basified with 3N-sodium hydroxide and the washed, dried precipitate (0·55 g.) was crystallised by dissolution in ethanol (1 ml. per g.) and slow dilution of the filtered solution with drops of water, affording *NN'*-diphenylguanidine, m. p. and mixed m. p. 147—149° (total, 0·38—0·51 g., 18—24% conversion).

Spontaneous evaporation of filtrate G to small volume at room temperature gave crystalline solid (0·06—0·1 g.) consisting of phenylthiourea and sulphur. The filtrate therefrom, after being strongly acidified with concentrated hydrochloric acid, slowly deposited oily droplets of phenylcyanamide, identified by conversion into the benzoyl derivative, m. p. 124—125° (from ethanol; 0·55 g., 25%) (Found: C, 75·6; H, 4·3. Calc. for $C_{14}H_{10}ON_2$: C, 75·7; H, 4·5%), by the Schotten–Baumann method [40% sodium hydroxide (20 ml.) and benzoyl chloride (5 ml.)].

Hydrolysis in boiling aqueous N-sodium hydroxide (30 ml.) during 10 min. gave a cruder product (2·2 g.) which was fractionated as above, affording the same products, though in somewhat lower yield.

3 : 5-*Di*-*imino*-2 : 4-*diphenyl*-1 : 2 : 4-*thiadiazolidine*.—(*a*) Phenylthiourea (30·4 g., 0·2 mole) in boiling ethanol (350 ml.) was treated with concentrated hydrochloric acid (20 ml., 0·2 mole), withdrawn from the heat source, and oxidised with 30% hydrogen peroxide (23 ml., 0·2 mole) (dropwise addition during 10—15 min.; the mixture boiled vigorously throughout); boiling was then continued for another 10 min. The cooled solution was decanted from the coagulated sulphur (3·0 g., 94%), diluted with water (1200 ml.), filtered (charcoal), and basified at 0° with ammonia. The dried precipitate (m. p. 183—184°, decomp., after sintering at 178°; 22—24 g., 82—90%) was crystallised from boiling methanol–acetone (1 : 1; 25—28 ml. per g.) and gave lustrous prisms, m. p. 184—185° (decomp.) (yield, 20·9—22 g., 78—82% in three successive crops).

(*b*) Phenylthiourea (0·2 mole) in boiling 50% ethanol (500 ml.) containing concentrated hydrochloric acid (5 ml.) was treated with 6% hydrogen peroxide (0·3 mole) during 20 min., the liquid refluxed for another 20 min., decanted from the sulphur, filtered (carbon), and basified with 20% sodium hydroxide (30 ml.), and the precipitate collected at once (Filtrate F). Crystallisation as above gave the thiadiazolidine in 43—52% yield. The warm filtrate F deposited lustrous crystals (m. p. 144—146°, 7—9%) on storage at 0°, which consisted of *sym*-diphenylguanidine, m. p. and mixed m. p. 146—148° (from 60% aqueous ethanol); more (6%) was isolated as the most soluble fraction in the crystallisation of the main product.

The yields of 1 : 2 : 4-thiadiazolidine from *p*-tolylthiourea obtained by procedure (*a*) and (*b*) were 50 and 30% respectively.

2 : 4-*Di*-p-*chlorophenyl*-3 : 5-*di*-*imino*-1 : 2 : 4-*thiadiazolidine*.—To a boiling solution of *p*-chlorophenylthiourea (7·46 g., 0·04 mole) in ethanol (40 ml.), concentrated hydrochloric acid (4 ml., 0·04 mole) was added, followed by 30% hydrogen peroxide (5 ml., 0·045 mole) with good mixing within 2—3 min. The swirled mixture was boiled during 3 min., and nearly filled with white solid. It was diluted with water (100 ml.) and concentrated hydrochloric acid (10 ml.), heated to boiling, and cooled to 0°. The collected product (7·35 g.) was extracted with successive portions of 50% aqueous acetone, and the undissolved coagulated sulphur (0·60 g., 94%) removed. The filtrate deposited crystals which were collected at 0° (6·4 g., 86%) and consisted, after a further crystallisation from 75% aqueous acetone, of prisms of **2 : 4-*di*-p-*chlorophenyl*-3 : 5-*di*-*imino*-1 : 2 : 4-*thiadiazolidine hydrochloride***, m. p. 265—266° (decomp., dependent on rate of heating) (Found: C, 44·7; H, 3·1. $C_{14}H_{10}N_4Cl_2S,HCl$ requires C, 45·0; H, 2·9%).

XUM

Alternatively, the crude hydrochloride (6·3 g.) was dissolved in nearly boiling water (350 ml.), and the solution basified with 3N-ammonium hydroxide. The precipitate (m. p. 165—167°; 5·4 g., 80%) was crystallised from ethanol (10 ml. per g.; with addition of a few drops of acetone) or from methanol–acetone (1 : 1, 2—3 ml. per g.). 2 : 4-*Di*-p-*chlorophenyl*-3 : 5-*di*-*imino*-1 : 2 : 4-*thiadiazolidine* had m. p. 167—168° (decomp.) (Found: C, 49·8; H, 2·9; N, 16·8; Cl, 20·8. $C_{14}H_{10}N_4Cl_2S$ requires C, 49·9; H, 3·0; N, 16·6; Cl, 21·05%).

The use of 6% hydrogen peroxide (0·04 mole) afforded, by the same procedure, the crude thiadiazolidine in 65% yield.

A solution of the 1 : 2 : 4-thiadiazolidine (0·5 g., 0·0015 mole) in acetic anhydride (10 ml.) was heated on the steam-bath during 0·5 hr., and the liquid then stirred into water. The precipitate (m. p. 204—205°, decomp.; 0·55 g., 96%) gave, after crystallisation from acetone–ethanol, glass-like prisms of the *monoacetyl derivative*, m. p. 207—209° (decomp.) (Found: C, 50·6; H, 3·3. $C_{16}H_{12}ON_4Cl_2S$ requires C, 50·7; H, 3·2%).

ROYAL FREE HOSPITAL SCHOOL OF MEDICINE
(UNIVERSITY OF LONDON), W.C.1.

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218. *Thiadiazoles. Part VII.*[1] 5-*Amino*-3-*mercapto*-1 : 2 : 4-*thiadiazole Derivatives.*

By FREDERICK KURZER and SHEILA A. TAYLOR.

1-Aryl(or alkyl)-4-alkyl*iso*-2 : 4-dithiobiurets are cyclised almost quantitatively by oxidising agents to 3-alkylthio-5-aryl(or alkyl)amino-1 : 2 : 4-thiadiazoles.

Some properties of this class of thiadiazole are described.

THE preceding Part [1] of this series described the oxidative ring-closure of 1-substituted 2-thiobiurets to 5-amino-3-hydroxy-1 : 2 : 4-thiadiazole derivatives. This general reaction [2] has now been extended to the synthesis of the analogous 3-alkylthio-heterocycles (II) from suitably substituted dithiobiurets (I). As before,[2] the cyclisation involves the dehydrogenation of the amidinothiono-grouping [·C(:NH)·NH·C(:S)·].

Although 1-substituted 2 : 4-dithiobiurets (VII) incorporate this system in their structure, they are, unlike 1-substituted 2-thiobiurets,[1] unsuitable as precursors of 1 : 2 : 4-thiadiazoles, since on oxidation their two potential mercapto-groups are preferentially affected, affording products that have been formulated [3] as 1 : 2 : 4-dithiazolidines (VIII). The reversible oxidation–reduction of the parent compound dithiobiuret (VII; R = H) and its oxidation product (VIII; R = H) has been similarly interpreted.[4] More recently, the possible alternative representation of oxidation products of dithiobiurets (VII; R = H or Ar) as 1 : 2 : 4-thiadiazoles (V) has been discussed by Bambas.[5] In the absence of further experimental results, however, the available evidence [3] appears to favour their cyclic disulphide (VIII) structure.[6] In the present work such structural uncertainties are avoided by the use of dithiobiurets in which one of the reactive sulphur atoms is blocked by an alkyl group. Of the two possible series of homologues, 1-substituted S^4- (I) and S^2-alkyl*iso*-2 : 4-dithiobiurets [R·NH·C(SR′):N·CS·NH_2], only the former, containing the amidinothiono-system, are convertible into 1 : 2 : 4-thiadiazoles.

Substituted dithiobiurets (I) required as starting materials were obtained by condensation of *iso*thiocyanates and *S*-alkyl*iso*thioureas by Johnson and Bristol's method.[7-9]

[1] Part VI, Kurzer and Taylor, *J.*, 1958, 379.
[2] Kurzer, *J.*, 1955, 1, and subsequent papers.
[3] Fromm, *Annalen*, 1893, **275**, 20, and subsequent papers; see also ref. 6.
[4] Preisler and Bateman, *J. Amer. Chem. Soc.*, 1947, **69**, 2632; Preisler, *ibid.*, 1949, **71**, 2849.
[5] Bambas, "The Chemistry of Heterocyclic Compounds," Interscience Publ. Inc., New York, 1952, Vol. IV, pp. 44—51.
[6] Kurzer, *Chem. Rev.*, 1956, **56**, 95, 154.
[7] Johnson and Bristol, *Amer. Chem. J.*, 1903, **30**, 172.
[8] Underwood and Dains, *Univ. Kansas Sci. Bull.*, 1936, **24**, 5.
[9] Birtwell, Curd, Hendry, and Rose, *J.*, 1948, 1645, 1654.

XUM

As in the corresponding synthesis of 1-substituted 2-thio-4-*iso*biurets,[1] the original procedure [7] was improved by performing the reaction in one phase at higher temperatures. Ethanol [9] was not used, however, because it tends to react with *iso*thiocyanates, particularly aromatic ones.[10] Boiling aqueous acetone, at various concentrations (cf. Experimental section), preferably with the addition of a tertiary base such as triethylamine as a catalyst, proved to be a satisfactory medium in all the cases studied. 1-Aryl-S[4]-alkyl(or aryl)*iso*-2 : 4-dithiobiurets (I; R = Ph, R′ = Me, CH_2Ph, or Ph) were thus obtained readily in 60—75% yields; 1-alkyl derivatives (I; R = Me, Pr^n, R′ = Me, or CH_2Ph), isolated as hydrochlorides because of the unfavourable physical properties of the free bases, were accessible in lower yields (25—45%) only. Methyl *iso*thiocyanate and *S*-methyl*iso*thiourea failed to react in the aqueous solvent, but afforded the required dithiobiuret (I; R = R′ = Me) under anhydrous conditions, in the presence of sodium as condensing agent. Unlike hydrochlorides of *O*-alkyl-1-methyl-2-thio*iso*biurets [NHMe·CS·NH·C(OAlk):NH,HCl], which are rapidly dealkylated in boiling solvents, salts of the present series of compounds (I) were purified without difficulty by crystallisation, since the corresponding thiohydrolysis of the S–alkyl link occurs only under special conditions.[8,9,11]

1-Substituted 4-*iso*-2 : 4-dithiobiurets (I) thus obtained were readily cyclodehydrogenated to homologues of 5-amino-3-mercapto-1 : 2 : 4-thiadiazole (II). Excess of hydrogen peroxide in the presence of mineral acid proved to be the superior oxidising agent, producing the heterocycles in 75—95% yield. The use of equimolecular proportions of bromine in organic solvents afforded the same products in somewhat lower yields. The halogen uptake was practically instantaneous, showing that ring closure occurred with almost ionic velocity: dithiobiuret (I) salts, which were insoluble in the usual non-polar solvents, were therefore readily oxidised in methanol, there being no significant halogen consumption in side-reactions with the solvent. Regardless of the nature of the medium used, however, certain dithiobiurets containing aromatic nuclei, particularly benzyl groups, tended to absorb more than the calculated quantity of bromine, probably because of slight losses of the reagent due to nuclear bromination: it is well established that benzene nuclei attached to amino- or substituted amino-groups are rapidly halogenated under the mildest conditions.[12] Certain dithiobiurets (I; R = Me, Pr^n, R′ = CH_2Ph) changed, in the presence of alkali, into the 1 : 2 : 4-thiadiazoles (II) merely in contact with air, demonstrating the remarkable ease with which this heterocyclic system is formed; similar observations are on record concerning the oxidation of thiobenzoylguanidine.[13]

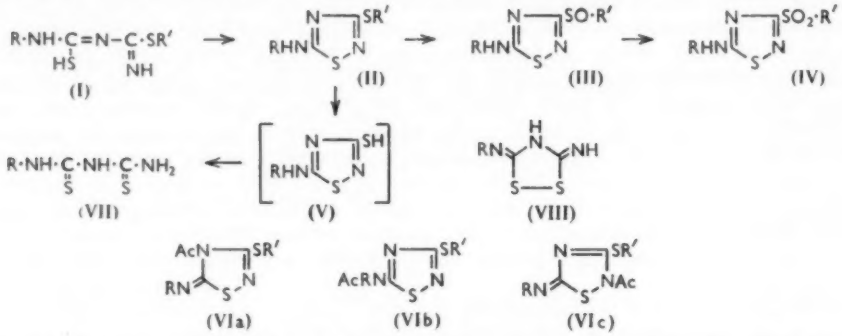
An alternative synthesis of 5-alkylamino-3-alkylthio-1 : 2 : 4-thiadiazoles, by the action of methyl- or benzyl-amine on 3-alkylthio-5-chloro-1 : 2 : 4-thiadiazoles, has been described by Goerdeler and Sperling.[14] The fact that representative examples of this series of compounds (II; R = Me, R′ = Me or CH_2Ph) prepared by both methods were identical further confirms the interpretation of the chemical changes involved in both syntheses.

The heterocyclic thiol derivatives (II) now synthesised showed properties in accord with their structure and, in particular, exhibited certain similarities with the corresponding oxy-compounds (cf. Part VI [1]). They were stable solids, which resisted desulphurisation by alkaline sodium plumbite, the heterocyclic nucleus being obviously stabilised [2] by the presence of the substituents. They were generally insoluble in acids and alkalis: 5-anilino-3-methylthio-1 : 2 : 4-thiadiazole, however, shared with the 3-amino- [2] and the 3-methoxy-analogue [1] the exceptional solubility in hot aqueous sodium hydroxide. 5-Anilino-3-methylthio-1 : 2 : 4-thiadiazole, like the 3-methoxy-analogue, gave a monoacetyl and a monobenzoyl derivative and failed to afford a toluene-*p*-sulphonyl derivative, as expected.

[10] Slotta, Tschesche, and Drechsler, *Ber.*, 1930, **63**, 208.
[11] Fairfull and Peak, *J.*, 1955, 796.
[12] See, for example, Robertson, de la Mare, and Swedlund, *J.*, 1953, 782.
[13] Goerdeler and Fincke, *Chem. Ber.*, 1956, **89**, 1033.
[14] Goerdeler and Sperling, *ibid.*, 1957, **90**, 892.

XUM

This provides yet another example of the frequently observed [1,2,15] lower reactivity of aminothiadiazoles towards sulphonyl halides than of acyl halides or anhydrides. For the reasons previously given in the oxy-series,[1] the site of substitution of the acyl group remains, for the time being, undecided, formulæ (VIa—c) being possible. In view of the known [16] greater reactivity of the 4- than of the 2-position in the 1 : 2 : 4-thiadiazole nucleus,



structure (VIc) can probably be ruled out. Alkylthio-groups in thiadiazoles (II) behaved normally in that their sulphur atom was convertible into the sulphoxyl or sulphonyl grouping; 5-anilino-3-methylthio-1 : 2 : 4-thiadiazole, for example, reacted with the appropriate quantities of monoperphthalic acid to give the sulphoxide or sulphone (III or IV; R = Ph, R′ = Me). Similar observations made with 5-amino-3-ethylthio-1 : 2 : 4-thiadiazole have been described by Goerdeler and Linden.[15]

The dealkylation of 3-alkylthio-5-anilino-1 : 2 : 4-thiadiazoles (II ⟶ V; R = Ph) was of special interest, since a comparison of authentic 5-anilino-3-mercapto-1 : 2 : 4-thiadiazole, if accessible by this method, with the oxidation product of 1-phenyldithiobiuret (" thiuret ") [3] would provide the information for a conclusive choice between the two possible structures (V, VIII) of the latter.[3,5] A widely applicable method for dealkylating methylthio-compounds, using hydrogen sulphide in pyridine–triethylamine, has recently been introduced by Fairfull, Lowe, and Peak,[17] and benzylthio-compounds have been converted into their parent thiols by du Vigneaud and his school [18] employing sodium in liquid ammonia. In the present series, however, the methylthio-compound and the benzyl analogue (II; R = Ph, R′ = Me or CH_2Ph) were converted directly into 1-phenyldithiobiuret by these methods. It is probable that the thiol (V; R = Ph) was formed in the first place, but was simultaneously ring-opened to the dithiobiuret (VII; R = Ph) under the reductive conditions of both dealkylation procedures. The ready reduction of 5-anilino-3-hydroxy-1 : 2 : 4-thiadiazole to 1-phenyl-2-thiobiuret [1] supports this view.

Experimental

Pyridine was the commercially available anhydrous grade. Light petroleum was of boiling range 60—80°.

The solvent used for preparing 1M-bromine was chloroform unless otherwise stated. Aqueous picric acid was used as 0·06M-solution (saturated at 30°).[19]

5-Arylamino-3-mercapto-1 : 2 : 4-thiadiazoles.—S[4]-*Methyl-1-phenyliso-2 : 4-dithiobiuret*, prepared in 60—75% yield by the method of Johnson and Bristol [7] (but in an aqueous acetone as described immediately below), formed needles, m. p. 123—124° (from benzene).

S[4]-*Benzyl-1-phenyliso-2 : 4-dithiobiuret.*—Benzyl*iso*thiuronium chloride (20·25 g., 0·1 mole)

[15] Goerdeler and Linden, *Chem. Ber.*, 1956, **89**, 2742.
[16] Goerdeler, Huppertz, and Wember, *ibid.*, 1954, **87**, 68.
[17] Fairfull, Lowe, and Peak, *J.*, 1952, 742.
[18] du Vigneaud *et al.*, *J. Amer. Chem. Soc.*, 1930, **52**, 4500; *J. Biol. Chem.*, 1935, **108**, 753; 1935, **109**, 97; 1935, **111**, 393; 1938, **123**, 327; Carter, Stevens, and Ney, *ibid.*, 1941, **139**, 247.
[19] Dolinski, *Ber.*, 1905, **38**, 1836.

was added to a solution of 5M-potassium hydroxide (20 ml., 0·1 mole), followed by acetone (75 ml.) and phenyl *iso*thiocyanate (10·13 g., 0·075 mole). The stirred suspension (later solution) was refluxed during 20—25 min. and added to ice-water (250 ml.), and the precipitated oil collected (when solidified at 0°) and air-dried. Crystallisation from benzene (150 ml.) gave needles (m. p. 115—117°; 15·6 g., 69%) of the *dithiobiuret*. Two further crystallisations from the same solvent afforded pale ivory needles, m. p. 116—118° (Found: C, 60·0; H, 5·3; N, 13·4; S, 21·8. $C_{15}H_{15}N_3S_2$ requires C, 59·8; H, 5·0; N, 13·95; S, 21·3%).

1-*Phenyl*-S[4]-*phenyl*iso-2 : 4-*dithiobiuret*.—A solution of *S*-phenyl*iso*thiourea [20] (7·6 g., 0·05 mole) in warm acetone (150 ml.) was treated with phenyl *iso*thiocyanate (6·75 g., 0·05 mole) and anhydrous triethylamine (1 ml.). The resulting yellow liquid was refluxed during 10 min., distilled to small volume (50 ml.), cooled, and stirred into ice-water (250 ml.). The solidified oil was broken up, collected, air-dried (11 g.), and successively crystallised from benzene (30 ml. per g.) and from chloroform–benzene (1 : 1), opaque needles of the *dithiobiuret*, m. p. 134—135°, being obtained [total yield, (here, and later, this term includes material from the mother-liquors), 10·05 g., 70%] (Found: C, 58·7; H, 4·7; N, 14·3; S, 21·7. $C_{14}H_{13}N_3S_2$ requires C, 58·5; H, 4·5; N, 14·6; S, 22·3%).

5-*Anilino*-3-*methylthio*-1 : 2 : 4-*thiadiazole*.—(*a*) A stirred solution of *S*[4]-methyl-1-phenyl-*iso*-2 : 4-dithiobiuret (2·25 g., 0·01 mole) in benzene (50 ml.) at 35—40° was treated, with external cooling, with bromine in chloroform (1M; 10 ml., 0·01 mole) which was rapidly decolorised. The separated crystalline precipitate was collected after 12 hours' storage at 0° (filtrate A) and dissolved in ethanol (120 ml.), the solution stirred into ice-water (500 ml.), and the product (m. p. 152—155°; 1·75—1·90 g., 80—85%) collected at 0°. Crystallisation from benzene (15 ml. per g., recovery 90%) gave needles of 5-*anilino*-3-*methylthio*-1 : 2 : 4-*thiadiazole*, m. p. 154—155° (Found: C, 48·9, 48·7; H, 4·1, 3·9; N, 18·9; S, 28·1. $C_9H_9N_3S_2$ requires C, 48·4; H, 4·0; N, 18·8; S, 28·7%). The benzene filtrates (A) gave only minute quantities (1—2%) of the same thiadiazole on evaporation. [Oxidation of the dithiobiuret (0·01 mole) in ethanol (40 ml.) as above resulted in lower yields (40%).]

(*b*) A solution of the reactant (0·03 mole) in ethanol (75 ml.) at 65° was treated dropwise with 6% hydrogen peroxide (51 ml., 0·09 mole) during 15 min. The crystals which separated were collected at 0° and rinsed with ethanol (m. p. 154—156°; 6·35 g., 95%); they consisted of almost pure 1 : 2 : 4-thiadiazole. The product was very sparingly soluble in boiling water, but very soluble in hot 3N-aqueous sodium hydroxide, and was deposited therefrom unchanged on cooling.

Derivatives. A solution of 5-anilino-3-methylthio-1 : 2 : 4-thiadiazole (1·12 g., 0·005 mole) in acetic anhydride (10 ml.) was boiled during 30 min., then added to water. The product, after crystallisation from acetone–ethanol, consisted of platelets (1·2 g., 90%) of the *monoacetyl derivative*, m. p. 204—206° (Found: C, 49·7; H, 4·1; N, 15·6. $C_{11}H_{11}ON_3S_2$ requires C, 49·8; H, 4·15; N, 15·85%). Interaction of the thiadiazole (0·005 mole) and benzoyl chloride (1·4 g., 0·01 mole) in pyridine (10 ml.) at 100° during 30 min., addition of the liquid to N-hydrochloric acid (120 ml.) at 0°, and crystallisation of the product from acetone–ethanol gave needles (90%) of the *monobenzoyl derivative*, m. p. 188—190° (Found: C, 59·0; H, 3·8; N, 12·8; S 20·1. $C_{16}H_{13}ON_3S_2$ requires C, 58·7; H, 4·0; N, 12·8; S, 19·6%). The thiadiazole did not yield a toluene-*p*-sulphonyl derivative by the usual procedure.[1]

3-(5-*Anilino*-1 : 2 : 4-*thiadiazolyl*) *Methyl Sulphoxide*.—A solution of 5-anilino-3-methylthio-1 : 2 : 4-thiadiazole (1·12 g., 0·005 mole) in chloroform (100 ml.) was treated at −30° (solid carbon dioxide–ethanol) with 0·2N-ethereal monoperphthalic acid [21] (50 ml., 0·005 mole) previously cooled to the same temperature. The solution, which deposited phthalic acid slowly, was stored at 0° during 24 hr., and at room temperature during 2 days, the oxidising agent then having been consumed (negative potassium iodide–starch test). The decanted colourless solution was evaporated in a vacuum at 35—45°, and the residue basified with 3N-sodium carbonate. The undissolved (solidified) residue (1·25 g.) was crystallised from ethanol (10 ml.), giving prisms (m. p. 146—147°; 0·87 g., 72%) which consisted, after further crystallisation from ethanol, and then from chloroform, of white opaque microcrystalline *sulphoxide*, m. p. 147—148° (Found: C, 45·3; H, 3·95; S, 27·8. $C_9H_9ON_3S_2$ requires C, 45·2; H, 3·8; S, 26·8%).

3-(5-*Anilino*-1 : 2 : 4-*thiadiazolyl*) *Methyl Sulphone*.—A solution of the reactant was similarly

[20] Arndt, *Annalen*, 1911, **384**, 322; 1913, **396**, 1, 6.
[21] Böhme, *Ber.*, 1937, **70**, 379; *Org. Synth.*, Coll. Vol. III, p. 619 (1955).

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treated at −30° with an excess of 0·2N-monoperphthalic acid [21] (200 ml., 0·02 mole). The reaction was exothermic. The liquid was kept at 0° during 24 hr., and at room temperature during 6 days, but excess of oxidant was still present. The decanted yellow liquid was treated as above, and the solidified oil crystallised from benzene–acetone. The resulting product (m. p. 138—143°; 0·82 g., 65%) gave, after further crystallisation from benzene and from ethanol–light petroleum, platelets of the *sulphone*, m. p. 140—141° (after sintering at 138°) (Found: C, 42·4; H, 3·65; N, 16·2; S, 26·2. $C_9H_9O_2N_3S_2$ requires C, 42·35; H, 3·5; N, 16·5; S, 25·1%).

1-*Phenyldi.hiobiuret.*—(a) *By demethylation of* 5-*anilino*-3-*methylthio*-1 : 2 : 4-*thiadiazole.* Through a solution of the reactant (2·23 g., 0·01 mole) in anhydrous pyridine (20 ml.)–triethylamine (1·1 g., 0·011 mole), kept at 48—52°, a slow stream of dry hydrogen sulphide (successive passage through calcium chloride and glycerol) was passed during 1·5 hr. More triethylamine (1 g., 0·01 mole) was added half-way through the reaction. The dark brown liquid was stirred into ice (30 g.) and concentrated hydrochloric acid (18 ml.), and the solidified pale yellow precipitate was collected at 0° and washed with water. The air-dried crude product (2·3 g.) was dissolved in 1·5N-sodium hydroxide (12 ml.), a small insoluble residue (mostly sulphur) removed, and the diluted stirred yellow filtrate (approx. 50 ml.) acidified (to pH 7—6) with 1·5N-hydrochloric acid. The white precipitate was collected at 0° (filtrate F), rinsed with water, air-dried [m. p. 164—166° (decomp.) after sintering at 160°; 1·9 g.], and crystallised from boiling methanol (25 ml. per g.) (a little undissolved sulphur being again removed), giving lustrous flakes of 1-phenyldithiobiuret, m. p. and mixed m. p. with authentic product [22–24] 166—168° [decomp., after sintering at 162°, subject to the rate of heating] (1·31 g., 62%). A specimen for analysis was further crystallised from boiling water, with the addition of a trace of sodium dithionite (Found: C 45·8; H, 4·3; N, 20·0; S, 30·8. Calc. for $C_8H_9N_3S_2$: C, 45·5; H, 4·3; N, 19·9; S, 30·3%). Evaporation of the methanolic filtrates in a vacuum under nitrogen gave further small crops of 1-phenyldithiobiuret, m. p. 162—166° (decomp.) (6—8%).

Filtrate F, on being acidified to pH 1, gave a yellow solid (0·4 g.) of indefinite m. p. [125—140° (decomp.)], from which up to one-third of its weight of 1-phenyldithiobiuret was obtainable by crystallisation from methanol.

Reducing the time of reaction to 1 hr. lowered the yield of the dithiobiuret to 40%. At room temperature, hydrogen sulphide in pyridine–triethylamine was without effect, the reactant being substantially recovered (65%) after 15 minutes' treatment.

(b) *By debenzylation of* 5-*anilino*-3-*benzylthio*-1 : 2 : 4-*thiadiazole.* To a solution of the reactant (2·99 g., 0·01 mole) in liquid ammonia (approx. 100 ml.), protected against atmospheric moisture, thin slices of sodium (0·92 g., 0·04 g.-atom) were added during 0·5 hr. with gentle shaking. The residual, nearly white solid (S) obtained on allowing the ammonia to volatilise at room temperature was dissolved in water (25 ml.) (with addition of a few drops of 3N-ammonia if necessary). The filtered liquid (removal of traces of floating oil) was acidified (to Congo Red) with 3N-hydrochloric acid (with addition of ice; slight evolution of hydrogen sulphide), and the precipitated white solid collected. It was fractionally reprecipitated (cf. section a), and the crude 1-phenyldithiobiuret so obtained (50—80%) crystallised from methanol, affording platelets (0·76 g., 36%), m. p. and mixed m. p. 165—166° (decomp.) (Found; C, 45·0; H, 4·5%).

The use of less sodium (0·02—0·03 g.-atom) and lower temperatures (external cooling by solid carbon dioxide–ethanol) gave a crude residue (S), the alkali-insoluble part of which was unchanged reactant [30—40%, m. p. and mixed m. p. 150—151° (from ethanol)], and correspondingly lower yields of the dithiobiuret.

The identity of 1-phenyldithiobiuret thus obtained was confirmed by its conversion, on condensation with benzaldehyde in the presence of hydrogen chloride, into hexahydro-1 : 2-diphenyl-4 : 6-dithiono-1 : 3 : 5-triazine [3,24] (in approx. 50% yield), m. p. and mixed m. p. with material prepared from authentic 1-phenyldithiobiuret [22,23] 217—219° (decomp.) (lit.,[3,24] m. p. 227°).

Widely differing m. p.s of 1-phenyldithiobiuret, ranging between 169° and 184° are given in the literature.[3,11,23,25] Our observations showed that this decomposition temperature was very dependent on the initial bath-temperature and the rate of heating. The m. p. (decomp.)

[22] Wunderlich, *Ber.*, 1886, **19**, 449.
[23] Hecht, *Ber.*, 1892, **25**, 749.
[24] Fairfull and Peak, *J.*, 1955, 803.
[25] Bousquet and Guy, U.S.P. 2,410,862.

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here given was obtained by inserting samples into the preheated bath at 150° and raising its temperature at approx. 5° per min.

5-Anilino-3-benzylthio-1 : 2 : 4-thiadiazole.—(a) Oxidation of *S*^{4}-benzyl-1-phenyl-*iso*-2 : 4-dithiobiuret (3·0 g., 0·01 mole) in benzene (75 ml.) [as described for the 4-methyl homologue] gave a crude product which was stirred with water (300 ml.), collected, and successively crystallised from a little acetone and ethanol, affording needles of the *thiadiazole*, m. p. 150—151° (total yield, 1·35 g., 45%) (Found: C, 60·8; H, 4·2; N, 13·8; S, 21·2. $C_{15}H_{13}N_3S_2$ requires C, 60·2; H, 4·35; N, 14·05; S, 21·4%).

(b) *By hydrogen peroxide oxidation.* *S*^{4}-Benzyl-1-phenyl*iso*-2 : 4-dithiobiuret (0·025 mole) in ethanol (80 ml.) was treated dropwise, at 65—75° during 10 min., with 6% hydrogen peroxide (42·5 ml., 0·075 mole), and the resulting crystalline suspension boiled during 5 min. The solid (m. p. 149—151°; 6·0—6·35 g., 80—85%), collected at 0° and crystallised as above, formed needles of the thiadiazole, m. p. and mixed m. p. 150—151°.

5-Anilino-3-phenylthio-1 : 2 : 4-thiadiazole. A solution of 1-phenyl-*S*^{4}-phenyl*iso*-2 : 4-dithiobiuret (2·87 g., 0·01 mole) in chloroform (70 ml.) decolorised bromine (1M; 10 ml., 0·01 mole) as rapidly as it was added. The clear liquid was evaporated in a vacuum, the residual solid (which smelled slightly of phenyl *iso*thiocyanate) treated with water (50 ml.), the suspension made just alkaline with 3N-sodium hydroxide, and the solid collected (2·5 g.). Successive crystallisation from benzene (25 ml. per g.) and ethanol (30 ml. per g.) gave lustrous needles of *5-anilino-3-phenylthio-1 : 2 : 4-thiadiazole*, m. p. 173—174° (total yield, 2·22 g., 78%) (Found: C, 58·9; H, 3·9; N, 15·0; S, 22·6. $C_{14}H_{11}N_3S_2$ requires C, 58·95; H, 3·9; N, 14·7; S, 22·45%).

5-Alkylamino-3-mercapto-1 : 2 : 4-thiadiazoles.—*1-Methyl-S*^{4}*-methyl*iso*-2 : 4-dithiobiuret.* Sodium (1·26 g., 0·055 mole) was introduced into acetone (50 ml.), and the resulting suspension treated with finely powdered methyl*iso*thiuronium sulphate (6·95 g., 0·05 mole), followed by methyl *iso*thiocyanate (3·65 g., 0·05 mole). The stirred mixture was refluxed during 30—40 min., the bulk of the acetone removed in a vacuum, and the residual two-phase system extracted with ether. The combined dried (Na_2SO_4) extracts were treated with 4N-ethanolic hydrochloric acid (12·5 ml., 0·05 mole). The precipitated solid was collected at 0°, washed with ether and dried in a vacuum [m. p. 189—192° (decomp.); 4·5 g., 45%]. Two crystallisations from methanol (25 ml. per g., followed by dilution with a little ether) gave clusters of needle-shaped *1-methyl-S*^{4}*-methyl*iso*-2 : 4-dithiobiuret hydrochloride*, m. p. 190—191° (decomp.) (Found: C, 23·9; H, 5·0; Cl, 17·5. $C_4H_9N_3S_2$,HCl requires C, 24·1; H, 5·0; Cl, 17·8%). The base, precipitated by alkali from an aqueous solution of the hydrochloride, formed oily droplets.

The *picrate*, obtained quantitatively, from aqueous solutions formed yellow prisms, m. p. 172—174° (from ethanol) (Found: C, 30·7; H, 2·8. $C_4H_9N_3S_2$,$C_6H_3O_7N_3$ requires C, 30·6; H, 3·1%).

S^4*-Benzyl-1-methyl*iso*-2 : 4-dithiobiuret.* To potassium hydroxide (85%, 1·65 g., 0·025 mole) in water (4 ml.) were successively added acetone (20 ml.), and a solution of benzyl*iso*thiuronium chloride (5·06 g., 0·025 mole) in warm water (15 ml.). The suspension was stirred until all had dissolved (addition of a little acetone, if necessary), methyl *iso*thiocyanate (1·8 g., 0·025 mole) added, and the stirred liquid refluxed during 1 hr., cooled, and stirred into water (200 ml.). The precipitated oil solidified slowly (72 hr.) on storage at 0°; it was collected, rinsed with water, and crystallised from benzene (15 ml.). The separated granular *dithiobiuret* (m. p. 93—96°; 1·50 g., 25%) consisted, after a further crystallisation from benzene of a white powder, m. p. 96—97° (Found: C, 50·2; H, 5·4; N, 17·8; S, 27·1. $C_{10}H_{13}N_3S_2$ requires C, 50·2; H, 5·4; N, 17·6; S, 26·8%). The benzene filtrate gave, on partial evaporation, small crops (0·27 g., 4·5%) of 3-benzylthio-5-methylamino-1 : 2 : 4-thiadiazole, m. p. and mixed m. p. with authentic material (see below) 139—141° (after further crystallisation from ethanol).

S^4*-Methyl-1-propyl*iso*-2 : 4-dithiobiuret.* To 5M-aqueous potassium hydroxide (0·05 mole), methyl*iso*thiuronium sulphate (6·95 g., 0·05 mole) dissolved in water (20 ml.) was added, followed by acetone (40 ml.) and propyl *iso*thiocyanate (5·05 g., 0·05 mole). The stirred liquid was refluxed during 40—50 min. and rapidly evaporated to small bulk under reduced pressure, and the crude hydrochloride [m. p. 179—180° (decomp., after sintering at 175°), 3·65 g., 32%] isolated as described for the lower homologue (in the present case the precipitate was exceptionally finely divided and was collected on hard filter-paper). Crystallisation from methanol (15 ml. per g., recovery 70%) gave lustrous flakes of *S*^{4}*-methyl-1-propyl*iso*-2 : 4-dithiobiuret hydrochloride*, m. p. 182—184° (decomp., somewhat subject to the rate of heating; inserted at 170°) (Found: C, 31·9; H, 6·1; N, 18·6; Cl, 15·9. $C_6H_{13}N_3S_2$,HCl requires C, 31·65; H, 6·15; N, 18·5; Cl, 15·6%). The hydrochloride was also recrystallisable from water. The free base,

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liberated from the aqueous hydrochloride, was a low-melting oil. Attempts to prepare a picrate (in aqueous or methanolic solution) gave only yellow gums.

The dithiobiuret gave a pale yellow precipitate with hot sodium plumbite (in 3N-sodium hydroxide); no lead sulphide was precipitated even on prolonged boiling.

S^4-*Benzyl*-1-*propyliso*-2 : 4-*dithiobiuret* was prepared (by the procedure detailed for the methyl homologue) by using benzyl*iso*thiuronium chloride (10·12 g., 0·05 mole); it was isolated by ether-extraction and precipitated as the hydrochloride [m. p. 171—172° (decomp.); 6·1 g., 40%]. Two crystallisations from methanol (15 ml. per g., recovery 60—70%) gave white flakes of *S*^{4}-*benzyl*-1-*propyliso*-2 : 4-*dithiobiuret hydrochloride*, m. p. 179—180° (decomp., after sintering at 174—176°; somewhat subject to the rate of heating; inserted at 170°) (Found: C, 47·7; H, 6·1; N, 13·4. $C_{12}H_{17}N_3S_2$,HCl requires C, 47·45; H, 5·9; N, 13·8%). Recovery of hydrochloride by evaporation (spontaneous, or in a vacuum) of the methanolic mother liquors was not practicable, small quantities of the corresponding 1 : 2 : 4-thiadiazole (presumably formed by atmospheric oxidation) being isolated in some of the experiments.

Attempts to prepare a picrate (in ethanolic solution) were unsuccessful, the hydrochloride being substantially recovered.

Treatment of the hydrochloride (0·0033 mole), suspended in water (20 ml.), with 3N-sodium hydroxide (0·0066 mole) and thorough grinding, gave an oil which solidified at 0°. It consisted, after crystallisation from light petroleum, of 3-benzylthio-5-propylamino-1 : 2 : 4-thiadiazole (54%), m. p. and mixed m. p. with authentic material (see below) 90—92°. [During the working-up and crystallisation, the product was exposed to air for prolonged periods.]

5-*Methylamino*-3-*methylthio*-1 : 2 : 4-*thiadiazole*. Addition of M-bromine (5 ml., 0·005 mole) to an externally cooled solution of 1-methyl-*S*^{4}-methyl*iso*-2 : 4-dithiobiuret hydrochloride (1·0 g., 0·005 mole) in methanol (25 ml.), followed by vacuum-distillation of the almost colourless liquid to half volume, addition to water (30 ml.), and basification with aqueous ammonia, gave a pale buff precipitate (m. p. 143—145°; 0·68 g., 85%). Three crystallisations from ethanol afforded colourless prisms of the thiadiazole, m. p. 144—145° (Found: C, 29·7; H, 4·4. Calc. for $C_4H_7N_3S_2$: C, 29·8; H, 4·35%). Goerdeler and Sperling [14] give m. p. 144·5—145° (sintering at 120°).

3-*Benzylthio*-5-*methylamino*-1 : 2 : 4-*thiadiazole*. Addition of M-bromine (0·005 mole) to a stirred solution of *S*^{4}-benzyl-1-methyl*iso*-2 : 4-dithiobiuret (1·2 g., 0·005 mole) in benzene (30 ml.) at 30° gave a creamy soft deposit, which later solidified. Its solution in ethanol (50 ml.) was diluted with water (200 ml.) and the precipitate collected after storage at 0° (m. p. 137—140°, after sintering at 130°; 0·72 g., 60%). Two crystallisations from ethanol gave needles of the thiadiazole, m. p. 139—140° (Found: C, 50·6; H, 4·9. Calc. for $C_{10}H_{11}N_3S_2$: C, 50·6; H, 4·6%). Goerdeler and Sperling give m. p. 139—140° (sintering at 125°).

3-*Methylthio*-5-*propylamino*-1 : 2 : 4-*thiadiazole*. Oxidation of *S*^{4}-methyl-1-propyl*iso*-2 : 4-dithiobiuret hydrochloride (1·14 g., 0·005 mole) in methanol (30 ml.) with M-bromine (0·005 mole), followed by vacuum-evaporation of the clear liquid (to 3 ml.), dilution with water (10 ml.), and basification with 3N-ammonia (10 ml.), gave an oil, which solidified at 0° (m. p. 64—67°; 0·86 g., 90%). Crystallisation from light petroleum (10 ml. per g.) and ethanol–water (1 : 1, 10 ml. per g.) gave needles of the *thiadiazole*, m. p. 68—70° (Found: C, 38·1; H, 5·85; N, 22·2. $C_6H_{11}N_3S_2$ requires C, 38·1; H, 5·8; N, 22·2%). The product is highly soluble in cold methanol, ethanol, and acetone. The *picrate*, prepared from hot saturated ethanolic solutions, formed yellow plates (85%), m. p. 138—139° (Found: C, 35·0; H, 3·3. $C_6H_{11}N_3S_2$,$C_6H_3O_7N_3$ requires C, 34·45; H, 3·35%).

3-*Benzylthio*-5-*propylamino*-1 : 2 : 4-*thiadiazole*. A solution of *S*^{4}-benzyl-1-propyl*iso*-2 : 4-dithiobiuret hydrochloride (1·52 g., 0·005 mole) in methanol (30 ml.) at 60° was treated with 6% hydrogen peroxide (8·5 ml., 0·015 mole) during 5 min., the clear liquid was boiled during 5 min., cooled somewhat, basified with ammonia, and diluted with water (30 ml.), and the needles were collected at 0°. Two crystallisations from light petroleum gave needles of the *thiadiazole*, m. p. 90—91° (total 1·0 g., 75%) (Found: C, 54·2; H, 5·5; N, 15·7; S, 23·9. $C_{12}H_{15}N_3S_2$ requires C, 54·3; H, 5·7; N, 15·85; S, 24·15%). The *picrate*, prepared from hot saturated ethanolic solution, formed yellow needles (75%), m. p. 131—132° (from ethanol) (Found: C, 43·9; H, 3·7. $C_{12}H_{15}N_3S_2$,$C_6H_3O_7N_3$ requires C, 43·7; H, 3·6%).

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ROYAL FREE HOSPITAL SCHOOL OF MEDICINE,
(UNIVERSITY OF LONDON), W.C.1.

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219. *Derivatives of Hydroxyquinol. Part I. Compounds Related to 3 : 4 : 6-Trimethoxy-2-propenylacetophenone.*

By F. M. Dean, D. R. Randell, and Graham Winfield.

The preparation and properties of several 5 : 6-disubstituted derivatives of hydroxyquinol related to certain fungal metabolites are described.

Apart from the 5-substituted derivatives, the chemistry of hydroxyquinol has not been systematically studied in spite of its importance in fungal metabolites [1] and depsidones: [2] this paper describes a general route to 5 : 6-disubstituted hydroxyquinols required for synthetical studies of citromycetin,[3] fulvic acid,[4] and ustic acid.[5]

Of the published routes [6-8] to ethers of 3 : 4 : 6-trihydroxyphthalic acid, that of MacKenzie and Robertson [8] employing the intermediate indanone (I; R = H) seemed suitable for extension, but the butyric acid (III), prepared from the æsculetin derivative [9] (II), gave only the dihydrocoumarin (IV) when attempts were made to convert it into the indanone (I; R = Me). Resistance to substitution in the 6-position of the hydroxyquinol nucleus was also evident in the phenolic ketone (V) (see below), this being inert in the Gattermann, Kolbe, and Reimer–Tiemann reactions and destroyed rather than nitrated by nitric acid. A similar resistance has already been noted [3] in the hydroxy-acid (VI) to Hoesch, Gattermann, and Friedel–Crafts conditions. Fortunately, the Claisen rearrangement, in which ionic demands are small,[10] is successful.

When modified by the use of boron trifluoride instead of aluminium chloride to induce the Fries rearrangement in the diacetate (VII), Mauthner's [11] preparation of 2 : 5-dihydroxy-4-methoxyacetophenone (VIII; R = H) from vanillin gave excellent yields of this phenol or of its monoacetate (VIII; R = Ac). Methylation and then hydrolysis of the acetate supplied the unreactive phenol (V). Selective alkylation of the quinol (VIII; R = H) to the benzyl ether (VIII; R = CH_2Ph), followed by treatment of the derived acetate with sodium hydride, furnished a β-diketone (IX) cyclised by hydrochloric acid to the chromone (X; R = CH_2Ph). More vigorous treatment of this chromone with hydrochloric acid supplied the corresponding 6-hydroxychromone (X; R = H) which was, however, more easily prepared by controlled hydrolysis of its 3-acetyl derivative (XI) obtained directly from the diacetate of 2 : 5-dihydroxy-4-methoxyacetophenone (VIII; R = H) by treatment with sodium hydride followed by acetic acid. The allyl ether (X; R = $CH_2{\cdot}CH{\cdot}CH_2$) of this hydroxychromone rearranged readily when heated, giving the desired 5-allyl-6-hydroxy-7-methoxy-2-methylchromone (XII; R = H). Unfortunately, the allyl group could not be isomerised into a propenyl group because the methyl ether (XII; R = Me) was destroyed by bases, and with acids suffered demethylation and cyclisation to the γ-pyronocoumaran (XIII).

Claisen rearrangement of the monoallyl ether (XIV; R = H) of 2 : 5-dihydroxy-4-methoxyacetophenone readily gave 2-allyl-3 : 6-dihydroxy-4-methoxyacetophenone (XV; R = H), and thence 3 : 6-dihydroxy-4-methoxy-2-propylacetophenone by hydrogenation. Monomethylation of this allylquinol was unusual because the chelated hydroxyl group was attacked preferentially, giving (XV; R = Me). This result may not be due entirely to

[1] Bracken, "The Chemistry of Micro-Organisms," Pitman, London, 1955.
[2] Asahina, in Zechmeister (Ed.), "Fortschritte der Chemie organischer Naturstoffe," Vol. 8, Springer-Verlag, Vienna, 1951.
[3] Robertson, Whalley, and Yates, *J.*, 1951, 2013.
[4] Dean, Eade, Moubasher, and Robertson, *J.*, 1957, 3497.
[5] Raistrick and Stickings, *Biochem. J.*, 1950, **48**, 53.
[6] Faltis and Kloiber, *Monatsh.*, 1929, **53**, 631.
[7] Bargellini, *Gazzetta*, 1914, **44**, I, 187.
[8] MacKenzie and Robertson, *J.*, 1949, 497.
[9] Vliet, in Gilman and Blatt (Ed.), "Organic Syntheses," Wiley and Sons, Inc., New York, 1941, Coll. Vol. I, p. 360.
[10] Tarbell, "Organic Reactions," Wiley and Sons, Inc., New York, 1944, **2**, 1.
[11] Mauthner, *J. prakt. Chem.*, 1933, **136**, 205.

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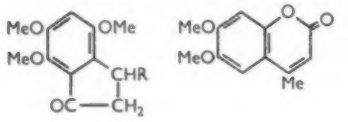
the hindered nature of the surviving hydroxyl group because some reduction in the stability of the chelated system must follow the partial rotation of the acetyl group necessary to accommodate the allyl substituent [see (XV)]. Vigorous alkylation of the quinol (XV; R = H) furnished the dimethyl ether, isomerised by bases into **3 : 4 : 6**-trimethoxy-2-propenylacetophenone (XVI; R = Me).

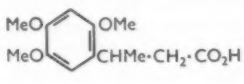
Similarly, benzylation and rearrangement of the allyl ether (XIV; R = H) led to the allylphenol (XVII; R = H), the methyl ether (XVII; R = Me) of which gave with bases 6-benzyloxy-**3 : 4**-dimethoxy-2-propenylacetophenone (XVI; R = CH_2Ph). This resinified in acid-catalysed debenzylation, but in catalytic hydrogenation gave 6-hydroxy-**3 : 4**-dimethoxy-2-propylacetophenone (XVIII).

The oxidation of the two propenylacetophenones (XVI; R = Me or CH_2Ph) was studied. The latter was destroyed by ozone, but the former gave a stable *iso*ozonide (XIX), the structure of which was inferred from its elementary analysis, the presence of two *C*-methyl groups (Kuhn–Roth), and the infrared spectrum, which indicated the

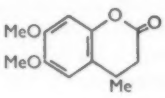


(I)

(II)

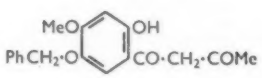


(III)

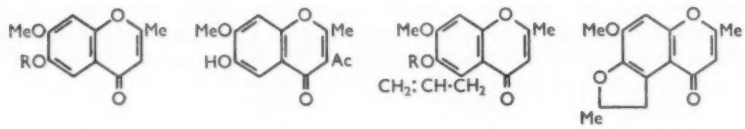


(IV)

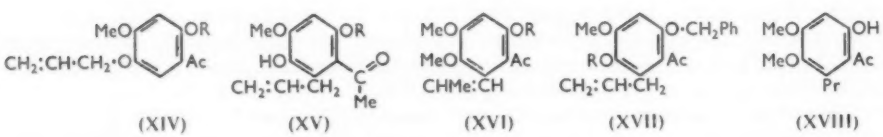
(V) (VI) (VII) (VIII)



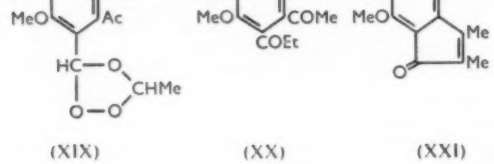
(IX)



(X) (XI) (XII) (XIII)



(XIV) (XV) (XVI) (XVII) (XVIII)



(XIX) (XX) (XXI)

presence of an acetophenone-type carbonyl group (1692 cm.$^{-1}$) (not reactive to hydroxylamine) and the absence of hydroxyl groups. Related compounds, *e.g.*, (XVIII), have three intense absorption bands, near 220, 270, and 300 mμ, but the *iso*ozonide has but one, at 303 mμ. This difference may have a stereochemical origin since models show that the

acetyl group in (XIX) cannot become coplanar with the benzene ring, and the crowding of the acetyl group and the *iso*ozonide system could account for the unusual stability of both. Under forcing conditions of either hydrolysis or reduction this *iso*ozonide gave resins only.

Both propenylacetophenones (XVI; R = Me or CH_2Ph) gave adducts with osmium tetroxide, but fission of these was accompanied by dehydration, resulting in a purple resin and the diketones (XX; R = Me or CH_2Ph), which gave a positive reaction (green turning violet) in the aniline acetate test [12] for *o*-diacylbenzenes, and phthalazines with hydrazine. Dehydration of (XX; R = Me) usually gave dark resins, but on one occasion gave a brick-red indenone (XXI) (C:O band at 1704 cm.$^{-1}$) thus confirming structures (XX; R = Me or CH_2Ph) for these diketones, both of which exhibited a single carbonyl band at 1700 cm.$^{-1}$.

Experimental

β-2 : 4 : 5-*Trimethoxyphenylbutyric Acid* (III).—A solution of 4 : *O* : *O*-trimethylæsculetin (10 g.) in 5% aqueous sodium hydroxide (100 ml.) was shaken under hydrogen with Raney nickel (5 g.) until colourless (~3 hr.). Liberated from the filtrate by hydrochloric acid and isolated with ether, β-2-*hydroxy*-4 : 5-*dimethoxyphenylbutyric acid* was obtained in needles (10 g.), m. p. 134°, from alcohol [Found: C, 59·9; H, 6·5; OMe, 25·7. $C_{10}H_{10}O_3(OMe)_2$ requires C, 60·0; H, 6·7; OMe, 25·8%]. Methyl sulphate (15·8 g.) was added with vigorous stirring to this acid (10 g.) in 10% aqueous sodium hydroxide (100 ml.) during ½ hr., and the whole boiled for 1 hr. Acidification of the cooled solution and extraction of the product into ether furnished β-2 : 4 : 5-*trimethoxyphenylbutyric acid*, crystallising from ether–light petroleum (b. p. 60—80°) in needles (9·5 g.), m. p. 102° [Found: C, 61·3; H, 7·1; OMe, 36·5, 36·6. $C_{10}H_9O_2(OMe)_3$ requires C, 61·4; H, 7·1; OMe, 36·6%]. This acid was hardly affected by polyphosphoric acid at 70°, by phosphoric oxide in boiling benzene, or by sulphuric acid monohydrate at 0°.

3 : 4-*Dihydro*-6 : 7-*dimethoxy*-4-*methylcoumarin* (IV).—The trimethoxy-butyric acid (III) (5 g.) was kept with phosphorus pentachloride (3·5 g.) in chloroform (75 ml.) for ¼ hr. at room temperature and then at 65° for ½ hr. The solvent was removed, and the residue freed from phosphorus oxychloride by repeated distillation of the benzene solution. The crude acid chloride was treated in stirred benzene (20 ml.) with powdered, freshly sublimed aluminium chloride (4·0 g.) at 30° and then kept at 80° for ½ hr. The mixture was decomposed with crushed ice (400 g.) and 2N-hydrochloric acid (200 ml.) and the product, isolated by repeated extraction with light petroleum, was purified from ether–light petroleum (b. p. 60—80°), giving 3 : 4-*dihydro*-6 : 7-*dimethoxy*-4-*methylcoumarin* in feathery rosettes (0·5 g.), m. p. 84°; ester absorption at 1740 cm.$^{-1}$ (Found: C, 64·9; H, 6·4. $C_{13}H_{14}O_4$ requires C, 64·9; H, 6·3%). Under milder conditions, only the butyric acid was recovered. Hydrolysis of the dihydrocoumarin by hot 2N-sodium hydroxide and acidification of the resulting solution with 0·5N-hydrochloric acid furnished β-2-hydroxy-4 : 5-dimethoxyphenylbutyric acid, m. p. and mixed m. p. 134°.

5-*Acetoxy*-2-*hydroxy*-4-*methoxyacetophenone* (VIII; R = Ac).—Vanillin (30 g.) in stirred N-sodium hydroxide (175 ml.) was cautiously oxidised with hydrogen peroxide (100-vol.; 30 ml.) in water (70 ml.). After 1½ hr. 10N-sodium hydroxide (60 ml.) and crushed ice (300 g.) were added, followed by acetic anhydride (50 ml.) with vigorous agitation. Methoxyquinol diacetate separated as a brown powder which, when purified from methanol, formed needles (33 g.), m. p. 94°, with a strong infrared absorption band (Nujol) at 1789 (phenolic acetate) (Found: C, 59·0; H, 5·5. Calc. for $C_{11}H_{12}O_5$: C, 58·9; H, 5·4%). Acetic acid (80 ml.) containing this diacetate (20 g.) was saturated with boron trifluoride and poured into water (300 ml.), whereupon 5-*acetoxy*-2-*hydroxy*-4-*methoxyacetophenone* slowly crystallised and was obtained by recrystallisation from alcohol as needles (18 g.), m. p. 104°, soluble in 2N-sodium hydroxide and having a purple ferric reaction in alcohol [Found: C, 58·6; H, 5·4; OMe, 14·0; OAc, 29·5. $C_6H_2O_2(OAc)(OMe)$ requires C, 58·9; H, 5·4; OMe, 13·9; OAc, 18·2%]. When the boron trifluoride reaction mixture was poured into 5N-hydrochloric acid (200 ml.) and boiled for ¼ hr., the cold solution deposited a brown powder, which, when crystallised from alcohol, gave 2 : 5-dihydroxy-4-methoxyacetophenone (VIII; R = H) in yellow needles (15·7 g.), m. p. 166°, having a green ferric reaction and infrared absorption bands (Nujol) at 3400 (C–OH) and 1675 cm.$^{-1}$ (chelated C:O)

[12] Weygand, Weber, and Maekawa, *Chem. Ber.*, 1957, **90**, 1879.

[Found: C, 59·4; H, 5·7; OMe, 17·3. Calc. for $C_9H_7O_3(OMe)$: C, 59·3; H, 5·5; OMe, 17·0%]. The *diacetate* formed needles, m. p. 130°, from a large volume of alcohol [Found: C, 58·7; H, 5·4; OMe, 12·0. $C_{12}H_{11}O_7(OMe)$ requires C, 58·6; H, 5·3; OMe, 11·7%].

5-Hydroxy-2 : 4-dimethoxyacetophenone (V).—5-Acetoxy-2-hydroxy-4-methoxyacetophenone (20 g.), potassium carbonate (20 g.), and methyl sulphate (10 ml.) were heated in boiling acetone (250 ml.) until a test sample gave no ferric reaction (~ 12 hr.). Evaporation of the hot filtrate to a small bulk (40 ml.) and addition of water (100 ml.) induced separation of the product which was purified from alcohol, giving *5-acetoxy-2 : 4-dimethoxyacetophenone* in prisms (20 g.), m. p. 123° [Found: C, 60·8; H, 6·1; OMe, 26·2. $C_{10}H_8O_3(OMe)_2$ requires C, 60·5; H, 5·9; OMe, 26·1%]. Hydrolysed in ½ hr. at 40° by sodium hydroxide (10 g.) in water (50 ml.), this acetate (7 g.) in alcohol (50 ml.) supplied the crude *phenol*, liberated by concentrated hydrochloric acid and purified from alcohol, forming prisms (5·5 g.), m. p. 154°, devoid of a ferric reaction [Found: C, 61·1; H, 5·8; OMe, 31·8. $C_8H_6O_2(OMe)_2$ requires C, 61·2; H, 6·2; OMe, 31·6%]. This phenol was unaffected by (i) hydrogen cyanide and zinc chloride (or aluminium chloride) in ether saturated with hydrogen chloride, (ii) aqueous potassium hydrogen carbonate at the b. p. for 1½ hr., (iii) sodium hydroxide and carbon tetrachloride under reflux for 18 hr.

5-Benzyloxy-2-hydroxy-4-methoxybenzoylacetone (IX).—Interaction of 2 : 5-dihydroxy-4-methoxyacetophenone (20 g.) and benzyl bromide (18·8 g.) in boiling acetone (350 ml.) containing potassium carbonate (20 g.) for 4 hr. gave *5-benzyloxy-2-hydroxy-4-methoxyacetophenone*, which was isolated in the usual way and then crystallised from chloroform–light petroleum, forming needles (20 g.), m. p. 151°, $\lambda_{max.}$ (in ethanol) 237, 277, 343 mμ (log ε 4·23, 4·05, 3·84), with a blue-green ferric reaction and giving a yellow solid with 2N-sodium hydroxide [Found: C, 70·4; H, 5·6; OMe, 11·5. $C_{15}H_{13}O_3(OMe)$ requires C, 70·6; H, 5·9; OMe, 11·4%]. With methyl sulphate and potassium carbonate in acetone, this phenol gave the 2 : 4-*dimethoxy-compound*, crystallising from aqueous alcohol in soft laminæ, m. p. 80°, turning pink in sunlight [Found: C, 71·3; H, 6·4; OMe, 21·8. $C_{15}H_{12}O_2(OMe)_2$ requires C, 71·3; H, 6·3; OMe, 21·7%]. The *acetate* formed needles, m. p. 100° from methanol [Found: C, 69·1; H, 5·9; OMe, 10·5. $C_{17}H_{16}O_4(OMe)$ requires C, 68·8; H, 5·7; OMe, 9·9%].

With sodium hydride (0·38 g.) in boiling pyridine (25 ml.) for ½ hr., 2-acetoxy-5-benzyloxy-4-methoxyacetophenone (5 g.) formed a solution which, when poured on ice (80 g.) containing a slight excess of acetic acid, gave a brown solid that separated from aqueous methanol, giving *5-benzyloxy-2-hydroxy-4-methoxybenzoylacetone* as needles (3·5 g.), m. p. 124°, soluble in dilute sodium hydroxide and having an olive-green ferric reaction (Found: C, 68·1; H, 5·6. $C_{18}H_{18}O_5$ requires C, 68·0; H, 5·3%). This diketone (6 g.) also resulted when 5-benzyloxy-2-hydroxy-4-methoxyacetophenone (10 g.) was refluxed with ethyl acetate (15 ml.) and sodium (8 g.) for 6 hr.

3-Acetyl-6-hydroxy-7-methoxy-2-methylchromone (XI).—The brown solution obtained from sodium hydride (0·4 g.) and 2 : 5-diacetoxy-4-methoxyacetophenone (5 g.) in boiling pyridine in ½ hr. was mixed with ice (100 g.) and acidified with acetic acid. The crystalline deposit was purified from methanol–benzene, giving the *3-acetylchromone* in needles (3 g.), m. p. 232°, soluble in dilute sodium hydroxide but devoid of a ferric reaction (Found: C, 61·7; H, 4·7. $C_{13}H_{12}O_5$ requires C, 62·9; H, 4·9%). The *acetate* separated from alcohol in needles, m. p. 210° (Found: C, 62·1; H, 5·0. $C_{15}H_{14}O_6$ requires C, 62·1; H, 4·9%), and the methyl ether in prisms, m. p. 192°, from benzene–light petroleum. Obtained by the potassium carbonate–acetone method, the *benzyl ether* crystallised from methanol–benzene in long needles, m. p. 179° (Found: C, 71·1; H, 5·5. $C_{20}H_{18}O_5$ requires C, 71·0; H, 5·3%), and when warmed on the steam-bath with acetic acid containing an equal volume of concentrated hydrochloric acid it regenerated the parent 3-acetylchromone, m. p. and mixed m. p. 232°.

6-Hydroxy-7-methoxy-2-methylchromone (X; R = H).—(i) The above 3-acetylchromone (XI) (1 g.) was heated under reflux for 3 hr. with 5% aqueous sodium carbonate (100 ml.). Liberated by dilute hydrochloric acid, *6-hydroxy-7-methoxy-2-methylchromone* crystallised from alcohol in needles (0·75 g.), m. p. 235° (Found: C, 64·1; H, 5·0. $C_{11}H_{10}O_4$ requires C, 64·1; H, 4·9%), giving the *acetate* as prisms, m. p. 162—164°, from alcohol (Found: C, 63·2; H, 4·9. $C_{13}H_{12}O_5$ requires C, 62·9; H, 4·9%).

(ii) When boiled vigorously for 2 min., diluted with water (20 ml.), and cooled, a solution of 5-benzyloxy-2-hydroxy-4-methoxybenzoylacetone (2 g.) in alcohol (20 ml.) containing concentrated hydrochloric acid (6 drops) slowly deposited *6-benzyloxy-7-methoxy-2-methylchromone*, which formed prisms (1·6 g.), m. p. 140°, from benzene–light petroleum [Found: C, 73·1; H, 5·8; OMe, 9·3. $C_{17}H_{13}O_3(OMe)$ requires C, 73·0; H, 5·4; OMe, 10·5%]. A mixture of this

chromone (0·25 g.), concentrated hydrochloric acid (4 ml.), and acetic acid (4 ml.) was kept at 90° for 1½ hr. and diluted with water. The product was purified from alcohol, giving the 6-hydroxychromone in needles (0·15 g.), m. p. and mixed m. p. 235°.

5-Allyl-6-hydroxy-7-methoxy-2-methylchromone (XII; R = H).—By means of allyl bromide (6·5 g.) and potassium carbonate (10 g.) in boiling acetone (125 ml.), 6-hydroxy-7-methoxy-2-methylchromone (10 g.) was converted into *6-allyloxy-7-methoxy-2-methylchromone* which, isolated by evaporation of the filtered solution and purified from aqueous methanol, formed pale yellow rhombs (11·5 g.), m. p. 125°, $\lambda_{max.}$ (in ethanol) 233, 280, 317 mμ (log ε 4·38, 3·95, 4·03) (Found: C, 68·3; H, 5·7. $C_{14}H_{14}O_4$ requires C, 68·3; H, 5·7%). When cooled, a solution of this 6-allyloxychromone (10 g.) in glycerol (100 ml.) which had been kept at 200° under nitrogen for ½ hr. deposited a solid which was recrystallised from alcohol giving *5-allyl-6-hydroxy-7-methoxy-2-methylchromone* in needles (9·6 g.), m. p. 216°, $\lambda_{max.}$ (in ethanol) 236, 281, 326 mμ (log ε 4·39, 3·94, 3·93) (Found: C, 68·1; H, 6·0. $C_{14}H_{14}O_4$ requires C, 68·3; H, 5·7%). The *acetate* (XII; R = Ac) formed silky needles, m. p. 125°, from aqueous alcohol (Found: C, 66·5; H, 5·5. $C_{16}H_{16}O_5$ requires C, 66·7; H, 5·6%). The *methyl ether* (XII; R = Me) (methyl sulphate–potassium carbonate) formed needles, m. p. 97°, from aqueous methanol, $\lambda_{max.}$ (in ethanol) ~230, 276, 307 mμ (log ε 4·41, 4·06, 3·96) (Found: C, 69·2; H, 6·1. $C_{15}H_{16}O_4$ requires C, 69·2; H, 6·2%).

7-Methoxy-2 : 6′-dimethyl-γ-pyrono(2′ : 3′-5 : 4)coumaran (XIII).—A rapid stream of hydrogen bromide was passed through 5-allyl-6 : 7-dimethoxy-2-methylchromone (500 mg.) in acetic acid (5 ml.). White crystals appeared after 1 hr.: these gradually redissolved. After 2 hr. the mixture was poured into water and neutralised with sodium hydrogen carbonate. The product (300 mg.) crystallised from aqueous methanol, giving the *γ-pyronocoumaran* in tiny prisms, m. p. 139°, $\lambda_{max.}$ (in ethanol) 218, 239, 336 mμ (log ε 4·36, 4·41, 3·87), insoluble in aqueous alkali, and inert to alcoholic ferric chloride and bromine in acetic acid [Found: C, 68·3; H, 5·9; OMe, 11·8; *C*-Me, 13·3. $C_{13}H_{11}O_3(OMe)$ requires C, 68·3; H, 5·7; OMe, 12·6; 2*C*-Me, 12·2%]. The same coumaran resulted when the allyldimethoxychromone was kept overnight at 0° in chloroform saturated with hydrogen bromide, and when 5-allyl-6-hydroxy-7-methoxy-2-methylchromone (XII; R = H) was treated with hydrogen bromide in acetic acid.

5-Allyloxy-2-hydroxy-4-methoxyacetophenone (XIV; R = H).—A mixture of 2 : 5-dihydroxy-4-methoxyacetophenone (20 g.), potassium carbonate (20 g.), and allyl bromide (13·6 g.) in acetone (250 ml.) was kept at the b. p. for 9 hr., then filtered and evaporated. The residue was recrystallised from light petroleum, giving *5-allyloxy-2-hydroxy-4-methoxyacetophenone* (XIV; R = H) in needles (20 g.), m. p. 80°, having a green ferric reaction (Found: C, 65·2; H, 6·5. $C_{12}H_{14}O_4$ requires C, 64·9; H, 6·4%). The *benzoate* (benzoyl chloride in 10% aqueous sodium hydroxide) crystallised in needles, m. p. 104°, from alcohol (Found: C, 69·9; H, 5·4. $C_{19}H_{18}O_5$ requires C, 69·9; H, 5·6%). The *acetate* (XIV; R = Ac) separated from benzene–light petroleum in needles, m. p. 116° (Found: C, 63·3; H, 5·9. $C_{14}H_{16}O_5$ requires C, 63·6; H, 6·1%), and the *methyl ether* (XIV; R = Me) (12 hours' alkylation by methyl sulphate–potassium carbonate) crystallised from the same solvent in needles, m. p. 81° (Found: C, 66·3; H, 7·0. $C_{13}H_{16}O_4$ requires C, 66·1; H, 6·8%).

2-Allyl-3-hydroxy-4 : 6-dimethoxyacetophenone (XV; R = Me).—(i) 5-Allyloxy-2 : 4-dimethoxyacetophenone (10 g.) was isomerised in boiling quinoline (50 ml.) during 40 min. and the product was isolated by dilution with ether (100 ml.), removal of quinoline by repeated washing with 5N-hydrochloric acid, and extraction into 2N-sodium hydroxide. Acidification of the extract and purification of the precipitate from benzene–light petroleum gave *2-allyl-3-hydroxy-4 : 6-dimethoxyacetophenone* (XV; R = Me) as needles (6·5 g.), m. p. 110° (Found: C, 65·9; H, 7·0. $C_{13}H_{16}O_4$ requires C, 66·1; H, 6·8%). A better yield (8·7 g.) resulted when the isomerisation was in glycerol at 200° and the product was isolated by addition of water.

(ii) Isomerisation of 5-allyloxy-2-hydroxy-4-methoxyacetophenone (10 g.) in glycerol (50 g.) as in (i) above but in a nitrogen atmosphere furnished *2-allyl-3 : 6-dihydroxy-4-methoxyacetophenone* (XV; R = H), crystallising from benzene–light petroleum in pale yellow needles (8·1 g.), m. p. 114°, having a transient green ferric reaction (Found: C, 65·0; H, 6·5. $C_{12}H_{14}O_4$ requires C, 64·9; H, 6·4%). Alkylation of this quinol (3 g.) with methyl iodide (1 mol.) and potassium carbonate in acetone gave 2-allyl-3-hydroxy-4 : 6-dimethoxyacetophenone (1·3 g.), m. p. and mixed m. p. 110°. Hydrogenation of this quinol (1 g.) in methanol (100 ml.) containing palladium–charcoal (0·5 g.) in the usual way supplied *3 : 6-dihydroxy-4-methoxy-2-propylacetophenone*, separating from aqueous alcohol in lime-green prisms (1 g.), m. p. 118°, $\lambda_{max.}$ (in ethanol)

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237, 277, 320 mμ (log ε 3·93, 3·59, 3·55) [Found: C, 64·1; H, 7·3; OMe, 14·1. $C_{11}H_{13}O_3(OMe)$ requires C, 64·3; H, 7·1; OMe, 13·8%].

3 : 4 : 6-*Trimethoxy*-2-*propenylacetophenone* (XVI; R = Me).—Methylation of either 2-allyl-3 : 6-dihydroxy-4-methoxyacetophenone or its 6-methyl ether (10 g.) with methyl sulphate and potassium carbonate gave **2-*allyl*-3 : 4 : 6-*trimethoxyacetophenone*** as an oil (10 g.), b. p. 110°/0·05 mm. (Found: C, 67·4; H, 7·0. $C_{14}H_{18}O_4$ requires C, 67·2; H, 7·3%). At 130° for 1 hr. in 25% methanolic potassium hydroxide followed by dilution with water (150 g.) this oil (10 g.) produced **3 : 4 : 6-*trimethoxy*-2-*propenylacetophenone***, which crystallised from light petroleum in needles (9·4 g.), m. p. 80° [Found: C, 67·3; H, 7·3; OMe, 36·4. $C_{11}H_9O(OMe)_3$ requires C, 67·2; H, 7·3; OMe, 37·2%].

2-*Allyl*-6-*benzyloxy*-3-*hydroxy*-4-*methoxyacetophenone* (XVII; R = H).—Isolated in the usual way from a mixture of 5-allyloxy-2-hydroxy-4-methoxyacetophenone (20 g.), benzyl bromide (8 ml.), and potassium carbonate (10 g.) which had been kept in boiling acetone for 12 hr., **5-*allyloxy*-2-*benzyloxy*-4-*methoxyacetophenone*** separated from light petroleum in needles (20 g.), m. p. 82°, $\lambda_{max.}$ (in ethanol) 235, 270, 328 mμ (log ε 4·35, 4·03, 3·91) (Found: C, 73·1; H, 6·4. $C_{19}H_{20}O_4$ requires C, 73·0; H, 6·3%), and when subjected (10 g.) to the Claisen rearrangement as for the analogues (XIV; R = H or Me) but in " Carbitol " at the b. p. for 1 hr. supplied **2-*allyl*-6-*benzyloxy*-3-*hydroxy*-4-*methoxyacetophenone*** as needles (8·9 g.), m. p. 116°, from benzene–light petroleum, soluble in 2N-sodium hydroxide [Found: C, 72·9; H, 6·3; OMe, 9·0. $C_{18}H_{17}O_3(OMe)$ requires C, 73·0; H, 6·3; OMe, 9·9%]. The ***methyl ether*** (XVII; R = Me) crystallised from light petroleum in soft plates, m. p. 50°, $\lambda_{max.}$ (in ethanol) 265, 296 mμ (log ε 3·58, 3·57), $\nu_{max.}$ 1689 (acetophenone C:O), 1645 and 1595 cm.$^{-1}$ (aromatic and double-bond) (Found: C, 73·9; H, 6·9. $C_{20}H_{22}O_4$ requires C, 73·6; H, 6·8%).

6-*Benzyloxy*-3 : 4-*dimethoxy*-2-*propenylacetophenone* (XVI; R = CH_2Ph).—2-Allyl-6-benzyloxy-3 : 4-dimethoxyacetophenone (5 g.) was heated in 25% methanolic potassium hydroxide (100 ml.) at 130° for 1 hr. The oil which separated when the mixture was poured on ice (180 g.) and kept, gradually solidified and could then be crystallised from aqueous methanol giving **6-*benzyloxy*-3 : 4-*dimethoxy*-2-*propenylacetophenone*** in rhombs (4·5 g.), m. p. 80°, $\lambda_{max.}$ (in ethanol 217, 235 (infl.), 309 mμ (log ε 4·53, 4·3, 3·58) [Found: C, 74·0; H, 7·2; OMe, 19·6. $C_{18}H_{16}O_3(OMe)_2$ requires C, 73·6; H, 6·8; OMe, 19·0%], with infrared absorption bands (Nujol) at 1695 (acetophenone C:O) and 1654 and 1595 cm.$^{-1}$ (aromatic and double-bond).

6-*Hydroxy*-3 : 4-*dimethoxy*-2-*propylacetophenone* (XVIII).—(i) Uptake of hydrogen ceased after absorption of 2 mol. when 6-benzyloxy-3 : 4-dimethoxy-2-propenylacetophenone (1 g.) in methanol (10 ml.) containing palladium–charcoal (0·5 g.) was shaken in this gas. Evaporation of the filtrate gave **6-*hydroxy*-3 : 4-*dimethoxy*-2-*propylacetophenone*** as a pale yellow oil, b. p. 160°/0·2 mm., $\lambda_{max.}$ (in ethanol) 218, 268, 306 mμ (log ε 4·12, 3·67, 3·60) [Found: C, 65·2; H, 7·7; OMe, 25·8. $C_{11}H_{12}O_2(OMe)_2$ requires C, 65·5; H, 7·6; OMe, 26·1%]. This phenol gave an intense green ferric reaction.

(ii) ½ Hr. after the gradual addition of 6-benzyloxy-3 : 4-dimethoxy-2-propenylacetophenone (1 g.) in ether (50 ml.) to calcium (0·5 g.) in liquid ammonia, ammonium chloride was added and the solvents were allowed to evaporate. The phenolic fraction of the residual brown gum was purified from benzene on neutral alumina, giving 6-hydroxy-3 : 4-dimethoxy-2-propylacetophenone, identified by means of its infrared spectrum with a specimen from (i).

3 : 4 : 6-*Trimethoxy*-2-*propenylacetophenone* iso*Ozonide* (XIX).—A stream of ozonised oxygen was passed into 3 : 4 : 6-trimethoxy-2-propenylacetophenone (3 g.) in ethyl acetate (90 ml.) at 0° for 2 hr. Removal of the solvent *in vacuo* left a gum which was unaffected by water and gave no reaction in the starch–iodide test but crystallised from aqueous methanol in plates (2·4 g.). Purified from benzene–light petroleum, this solid furnished the ***isoozonide*** in prisms, m. p. 116—118°, $\lambda_{max.}$ (in ethanol) 303 mμ (log ε 3·66), insoluble in 2N-sodium hydroxide, devoid of a ferric reaction, and inert to alkaline silver oxide [Found: C, 56·4, 56·4, 56·4; H, 6·3, 6·4, 6·1; OMe, 30·9; *C*-Me (Kuhn–Roth), 9·5. $C_{14}H_{18}O_7$ requires C, 56·4; H, 6·1; OMe, 31·2; 2*C*-Me, 10·1%].

3 : 4 : 6-*Trimethoxy*-2-*propionylacetophenone* (XX; R = Me).—The adduct which separated overnight from mixed solutions of osmium tetroxide (3·5 g.) in ether (50 ml.) and of 3 : 4 : 6-trimethoxy-2-propenylacetophenone (3·5 g.) was decomposed in aqueous methanol (50 ml.) by sulphur dioxide. Filtered through charcoal, the solution was concentrated under reduced pressure and extracted continuously with ether, from which evaporation left a gum; purification from a little methanol and then light petroleum gave the ***propionylacetophenone*** as prisms,

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m. p. 94—97°, $\lambda_{max.}$ (in ethanol) 215, 230, 270, 321 mμ (log ε 4·16, 4·14, 3·92, 3·91) (Found: C, 63·5; H, 6·9. $C_{14}H_{18}O_5$ requires C, 63·2; H, 6·8%).

With hydrazine hydrochloride (100 mg.) and sodium acetate (150 mg.) in water (1 ml.) at 80° for 10 min., this diketone (100 mg.) in alcohol (2 ml.) gave a solid, which, when treated with 2N-aqueous sodium hydroxide and crystallised from aqueous methanol, furnished *4-ethyl-5 : 6 : 8-trimethoxy-1-methylphthalazine* in needles, m. p. 120° (Found: C, 64·0; H, 7·0; N, 10·6. $C_{14}H_{18}O_3N_2$ requires C, 64·1; H, 6·9; N, 10·7%).

6-Benzyloxy-3 : 4-dimethoxy-2-propionylacetophenone (XX; R = CH_2Ph).—As with the trimethoxy-analogue, 6-benzyloxy-3 : 4-dimethoxy-2-propenylacetophenone (2 g.) formed with osmium tetroxide an adduct which, when decomposed by sulphur dioxide in 80% alcohol containing charcoal, gave a reddish solid. Extraction of this solid with ether left a gum from which boiling light petroleum (b. p. 60—80°) isolated material which, purified from benzene–light petroleum, gave *6-benzyloxy-3 : 4-dimethoxy-2-propionylacetophenone* in prisms (800 mg.), m. p. 111° [Found: C, 70·3; H, 6·3; OMe, 13·6; *C*-Me (Kuhn–Roth), 7·8. $C_{18}H_{16}O_3(OMe)_2$ requires C, 70·2; H, 6·4; OMe, 18·0; 2*C*-Me, 8·8%]. This diketone with hydrazine gave *8-benzyloxy-4-ethyl-5 : 6-dimethoxy-1-methylphthalazine*, crystallising from benzene in needles, m. p. 137° (Found: C, 71·1; H, 6·6. $C_{20}H_{22}O_3N_2$ requires C, 71·0; H, 6·5%).

4 : 6 : 7-Trimethoxy-2 : 3-dimethylindenone (XXI).—Heating of 3 : 4 : 6-trimethoxypropionylacetophenone (2 g.) with acetic anhydride (35 ml.) and sodium acetate (2·5 g.) in the steam-bath for 1½ hr. gave a dark solution which was poured into water (80 ml.). Next day the residual red gum solidified in contact with ether and when crystallised from benzene–light petroleum supplied the *indenone* in massive red prisms, m. p. 174° (Found: C, 68·0; H, 6·4. $C_{14}H_{16}O_4$ requires C, 67·7; H, 6·5%). Small quantities of this indenone often accompanied the diketone formed by decomposition of the osmic ester, but no conditions have been found in which the cyclisation occurs reliably.

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UNIVERSITY OF LIVERPOOL. [*Received, October 22nd*, 1958.]

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220. *High-temperature Phase Equilibria in the System Dicalcium Silicate–Tricalcium Phosphate.*

By R. W. NURSE, J. H. WELCH, and W. GUTT.

High-temperature phase equilibria in the system $2CaO,SiO_2$—$3CaO,P_2O_5$ have been investigated by high-temperature microscopy and *X*-ray analysis. The system presents a continuous series of solid solutions with a melting-point maximum at 2240°, contradicting earlier findings. A new high-temperature form of $3CaO,P_2O_5$ has been discovered which does not survive quenching to room temperature, but is completely miscible with the α form of $2CaO,SiO_2$. At lower temperatures two compounds are formed by solid-state reactions, the known silicocarnotite stable below 1450° and a new phase, denoted as " A," stable below 1125°, having the approximate composition $7CaO,P_2O_5,2SiO_2$. Powder *X*-ray measurements are given for each phase in the system, either as obtained in a specially designed high-temperature *X*-ray camera or, where appropriate, as recorded at room temperature in a focusing camera.

THE section $2CaO,SiO_2$—$3CaO,P_2O_5$ in the ternary system $CaO–SiO_2–P_2O_5$, which is relevant to processes in the steel, cement, and fertiliser industries, has been examined [1-5] with widely differing conclusions. This divergency can be attributed to the experimental

[1] Trömel, *Stahl und Eisen*, 1943, **63**, 21.
[2] Barrett and McCaughey, *Amer. Mineralogist*, 1942, **27**, 680.
[3] Bredig, *J. Phys. Chem.*, 1942, **46**, 747.
[4] Trömel, Harkort, and Hotop, *Z. anorg. Chem.*, 1948, **256**, 253.
[5] Berak and Wojciechowska, *Roczniki Chem.*, 1956, **30**, 757.

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difficulties. There are two main problems. First, as the liquidus temperatures over a large part of the system exceed 2000° C, accurate temperature measurement and detection of the liquidus are difficult. For instance, observation of external collapse of a specimen during heating, while a guide to the solidus temperature in the absence of impurities, provides a very unreliable indication of the liquidus. Trömel *et al.*[4] tried to obtain a more exact indication of the liquidus by stirring their melts with an iridium wire, but they make no pretensions to very great accuracy with this method. Secondly, reliance was placed on *X*-ray identification of quenched materials in the belief that rapid cooling would preserve the equilibrium products present at high temperature. At the outset it became apparent that this technique, although widely employed, is not applicable to the system $2CaO,SiO_2$—$3CaO,P_2O_5$ since some of the phases do not survive quenching. These difficulties were overcome.

Experimental

We adopted a method of high-temperature microscopy, which permits continuous observation of the behaviour of melts, described by Welch.[6] It employs a small electrically heated thermocouple to serve as specimen holder, heater, and thermometer. The couple is mounted on the stage of a polarising microscope used to study the material at the junction. The highest temperature attainable with the original apparatus with platinum–rhodium thermocouples (20% Rh, 80% Pt/40% Rh, 60% Pt) is 1880°, which is below the liquidus temperature in much of the present system.

Much higher temperatures were achieved with a tungsten–molybdenum thermocouple but although such couples are easily made, and oxidation can be prevented by use of an argon atmosphere, these highly reactive metals are attacked by the materials to be examined. The technique finally adopted was basically that described by Welch and Gutt,[7] the thermocouple being replaced by a heating element of pure iridium in a gas-tight cell through which dry argon circulated.

Further improvements concern the method of measuring the temperature of the heater. This was recorded in terms of r.m.s. current through it, the relation between current and temperature being established at the m. p.s of pure compounds such as Al_2O_3, MgO,Al_2O_3, and CaO,SiO_2. The use of optical pyrometry was explored but the disappearing filament pyrometer had to be sighted through the glass window of the cell housing the heater, and even slight clouding of this by volatilised substances seriously affected the measurements. However, this method was used to check the accuracy of the current calibration as follows: the brightness temperature at the m. p. (taken as 2454° * [8]) of the iridium heater, as observed through the glass window, was measured, and the effective spectral emissivity calculated by the relationship:

$$\frac{1}{T} - \frac{1}{S} = \frac{\lambda\,(\log e_\lambda)}{0{\cdot}4343c_2}$$

where T = true temperature (°K), S = brightness temperature (°K), $\lambda = 0{\cdot}65\ \mu$, $c_2 = 14{,}320\ \mu$ deg., e_λ = spectral emissivity at wavelength λ. If we assume that over the measurable range of brightness temperature this value of emissivity remains constant, the corresponding true temperature could similarly be derived from any brightness temperature. It was thus possible to check directly the m. p.s of a number of pure oxides, and for the great majority the agreement was within $\pm 10°$ of the values in the literature. This check confirmed the validity of assuming a constant value of emissivity for the iridium heater, and at the same time indicated which of the pure oxide preparations gave the most reproducible m. p.s for calibration.

Volatilisation was considered; depending on the initial composition differential loss of either P_2O_5 or CaO could occur during thermal treatment. For instance, after several minutes' heating, $2CaO,P_2O_5$ changes into $3CaO,P_2O_5$ through loss of P_2O_5, but in a few hours' heating $4CaO,P_2O_5$ loses lime, also becoming $3CaO,P_2O_5$. $3CaO,P_2O_5$ appeared to be particularly

* All temperatures given in this paper refer to the International Temperature Scale of 1927.

[6] Welch, *J. Sci. Instr.*, 1954, **31**, 458.
[7] Welch and Gutt, *J. Amer. Ceramic Soc.*, 1959, in the press.
[8] Henning and Wensel, *Bur. Stand. J. Res.*, 1933, **10**, 809.

stable. To test the volatilising behaviour of the $3CaO,P_2O_5$–$2CaO,SiO_2$ mixes, specimens of composition close to the highest-melting mixes were melted on the iridium wire, and maintained above the m. p. for a period considerably exceeding that needed for liquidus determination. By repetition enough material was collected for analysis which showed that the composition had not changed.

The dynamic method of optical examination used permitted the determination of the liquidus, that is, the temperature at which the smallest observable crystal could be maintained

TABLE 1. *Characteristic X-ray powder measurements for the high-temperature continuous solid solution series* $2CaO,SiO_2$—$3CaO,P_2O_5$.

$2CaO,SiO_2$ ...	100		94·4		91·6		83·3		80		75·9		69·0	
$3CaO,P_2O_5$ ...	0		5·6		8·4		16·7		20		24·1		31·0	
Temp.	1550°		1450°		1350°		1500°		1500°		1500°		1500°	
	d	*I*	*d*	*I*	*d*	*I*	*d*	*I*	*d*	*I*	*d*	*I*	*d*	*I*
	4·00	1	4·03	1	4·00	1	4·03	1	4·00	2	3·97	2	3·95	2
	3·63	1	3·67	1	3·69	1			3·71	2	3·69	4	3·69	1
	2·89	5	2·91	8	2·91	8	2·91	5	2·91	4	2·90	8	2·90	6
	2·74	4	2·76	8	2·77	8	2·75	4	2·75	5	2·73	7	2·73	6
	1·99	1	2·00	4					2·00	3	1·99	4	1·99	2

$2CaO,SiO_2$ ...	66·0		62·5		56·4		50·7		45·6		40·4	
$3CaO,P_2O_5$ ...	34·0		37·5		43·6		49·3		54·4		59·6	
Temp.	1200°		1500°		1500°		1500°		1500°		1500°	
	d	*I*	*d*	*I*	*d*	*I*	*d*	*I*	*d*	*I*	*d*	*I*
	3·95	3	4·00	2	4·03	2	3·99	3	3·99	3	4·00	3
	3·64	2	3·74	1	3·78	1	3·75	2	3·77	1	3·80	1
	2·88	8	2·93	8	2·97	6	2·94	8	2·95	8	2·94	8
	2·72	7	2·74	2	2·76	5	2·73	7	2·73	7	2·72	7
			1·99	2			2·00	5	2·00	4	1·99	1

$2CaO,SiO_2$ ...	34·9		27·4		19·2		12·2		5·8		0	
$3CaO,P_2O_5$ ...	65·1		72·6		80·8		87·8		94·2		100	
Temp.	1500°		1550°		1400°		1500°		1500°		1500°	
	d	*I*	*d*	*I*	*d*	*I*	*d*	*I*	*d*	*I*	*d*	*I*
	3·98	4	4·03	4	3·98	3	3·97	4	3·96	4	3·96	8
			3·83	1	3·81	1			3·83	1	3·84	1
	2·94	6	2·97	7	2·94	8	2·95	6	2·95	8	2·96	10
	2·70	4	2·73	5	2·71	7	2·69	5	2·67	6	2·68	9
	1·99	3	1·96	1			1·98	1	1·98	2	1·98	6

Compositions are % w/w. The high-temperature camera had diam. 102 mm., and Cu-K_α radiation was used. Interplanar spacings (*d*) are given in Å. Relative intensities (*I*) are estimated visually on an arbitrary scale from 1 (very weak) to 10 (very strong).

in the melt without growth or decay. It was also possible to recognise the occurrence of polymorphic transformations and optical changes occurring during cooling or heating of compositions within the system. There remained however the problem of identifying the unquenchable phases and of exploring the temperature region below about 1000° where some of the materials became opaque and changes occurring on further cooling could not be followed optically. In order to follow more closely the sub-solidus phase relations the heated stage equipment was adapted to form the basis of an *X*-ray camera capable of recording powder diffraction patterns up to 1850°. This has been described fully elsewhere;[9] essential data are under Table 1.

The mixes were prepared from crushed quartz (99·95% pure), calcium carbonate (99·9% pure), and $2CaO,P_2O_5$ (≮99·9% pure) made from " AnalaR " phosphoric acid and $CaCO_3$. The powdered materials, which had been screened through a 100-mesh sieve, were mixed dry and ignited in platinum boats at 1000° and subsequently at 1550° in an electric furnace for 20 hr.

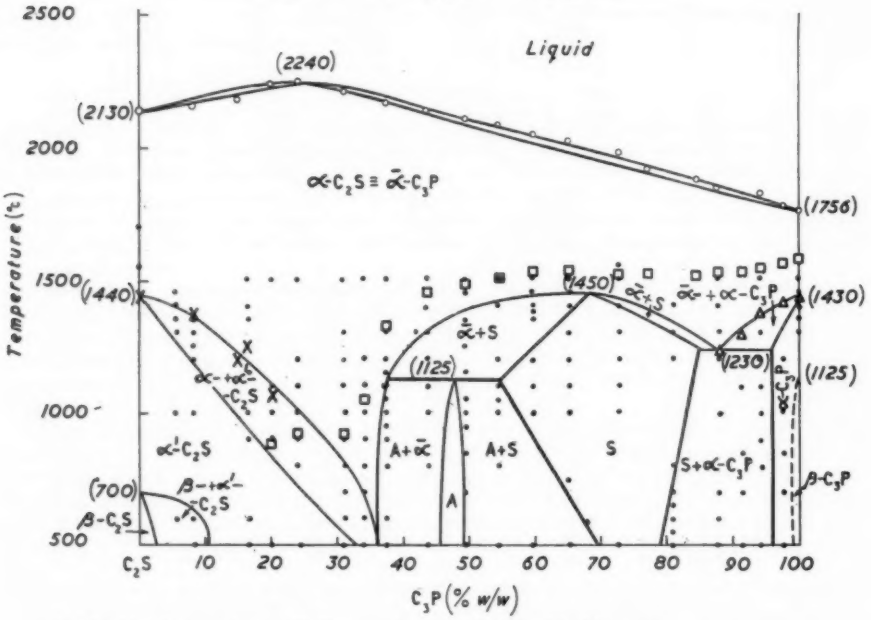
RESULTS AND DISCUSSION

The liquidus curve, determined with the thermocouple up to 1880° and on the iridium wire at higher temperatures, is shown in the Figure. In contradiction to the views of earlier

[9] Aruja, Welch, and Gutt, *J. Sci. Instr.*, 1959, **36**, 16.

workers already mentioned, the system presents a continuous series of solid solutions with a m. p. maximum of 2240° at 24% of $3CaO,P_2O_5$. The solidus curve was more difficult to establish. First, it is known that traces of impurity depress the temperature of initial melting far more markedly than the liquidus temperature; secondly, the readiness with which the first traces of liquid could be observed made it difficult to distinguish between slight initial liquid formation due to impurities, and the onset of a major degree of melting, signifying that the real solidus temperature had been reached. In addition, the calibration curve of the iridium heater was based on temperatures at which the last surviving crystals

The system $2CaO,SiO_2(C_2S)$–$3CaO,P_2O_5(C_3P)$.



○ Liquidus temperature. □ Temperature of minimum birefringence.
△ Temperature of $\tilde{\alpha} \longrightarrow \alpha$ transition of $3CaO,P_2O_5$, by optical determination.
× Temperature of $\alpha \longrightarrow \alpha'$ transition of $2CaO,SiO_2$, by optical determination.
● Points at which determinations were made with the high-temperature *X*-ray camera.

A is a new phase, and S is silicocarnotite.

could be maintained at the centre of the melt, whereas the temperature gradient in the specimen first formed liquid at points closest to the wire. This problem was dealt with by Welch and Gutt,[7] who described a possible method of correction. However, we have not included the experimental determinations of the solidus as they were not considered to be sufficiently reproducible. Accordingly a hypothetical solidus curve is shown on the phase diagram. The maximum in the liquidus curve indicates a tendency towards compound formation and the *X*-ray investigation at lower temperatures confirms the existence of two compounds.

Also shown in the Figure are certain optical observations made during heating and cooling below the m. p. When $3CaO,P_2O_5$ cooled from the m. p. (1756°) the birefringence first decreased to a minimum (1577°) whereat the specimen appeared isotropic and the sign of elongation changed. On further cooling the birefringence increased slowly until an abrupt increase took place at about 1430°. This was followed by a further gradual

increase usually accompanied by cracking due to thermal shock as room temperature was approached. The temperatures of the minimum and the sudden increase in birefringence were fully reproducible. Examination of compositions lying on the join $2CaO,SiO_2$–$3CaO,P_2O_5$ revealed that the sudden increase in birefringence could be observed up to 12% of $2CaO,SiO_2$ at successively lower temperatures. The minimum birefringence stage was observable with all compositions up to 80% of $2CaO,SiO_2$. At this composition the temperature of the minimum was lower than for pure $3CaO,P_2O_5$. There was a continuous tendency for the temperature of the minimum to fall as the $2CaO,SiO_2$ content increased. Its value for individual compositions was fully reproducible and was best determined after cooling the specimen from above the liquidus as rapidly as possible, in order to prevent fractional recrystallisation. This method of cooling also minimised cracking; when this occurred the birefringence minimum was less easily seen in the fragments.

With pure $2CaO,SiO_2$ the polymorphic inversions from α to α' and then to β could be seen. The former was particularly striking, being accompanied by an overall contraction of the material as well as by a marked change in birefringence. The α' to β inversion was characterised by a slight increase in birefringence readily observable provided the orientation of the crystals was favourable. The β—γ transformation, when it occurred, was characterised by abrupt opacification and distintegration. As $3CaO,P_2O_5$ was added the temperature of the α—α' inversion was lowered, reaching the lowest value observable with certainty at 20% of $3CaO,P_2O_5$. This composition was also the richest in $2CaO,SiO_2$ which exhibited the minimum in birefringence (Figure).

The sudden increase in birefringence for $3CaO,P_2O_5$ is regarded as coincident with a transformation from a hitherto unobserved higher-temperature form (hereafter called super-α-$3CaO,P_2O_5$) into what was previously regarded as the highest-temperature form (α-$3CaO,P_2O_5$). Super-α-$3CaO,P_2O_5$ cannot be preserved at room temperature. In order not to cause confusion with the $2CaO,SiO_2$ series of inversions this new $3CaO,P_2O_5$ phase will be written as $\bar{\alpha}$-$3CaO,P_2O_5$.

The minimum birefringence is not considered as indicating a polymorphic transformation, but as arising through a differential thermal expansion in two crystallographic directions. Its significance was that in the early stages of this work it suggested that a continuous phase existed over a portion of the system represented by all previous investigators as having a discontinuity of the solid phase. These views are supported by *X*-ray analysis in the high-temperature camera. The patterns obtained at 1500° with all the compositions lying on the join $2CaO,SiO_2$–$3CaO,P_2O_5$ were consistent with the behaviour of a continuous series of solid solutions. These patterns, which were essentially of the same type, were characterised by two strong lines whose separation increased systematically as $2CaO,SiO_2$ was added to $3CaO,P_2O_5$. The *d* values for the five strongest lines recorded at high temperatures over the entire composition range are given in Table 1. Two additional lines, of medium intensity at 3·1 Å and 3·5 Å (not shown), were also observed over the limited composition range 49—72% of $3CaO,P_2O_5$.

Apart from the inversions already described, dusting of the material during cooling was observed on the hot stage in the composition range 50—90% of $3CaO,P_2O_5$, the specimen simultaneously becoming opaque. *X*-Ray analysis of the dust showed that this change was associated with the formation of silicocarnotite. To establish the phase relations at the lower temperatures a systematic *X*-ray analysis was carried out in the high-temperature camera, the temperatures and compositions being chosen on the basis of the microscopical information. Additional high-temperature powder diffraction data for the intermediate polymorphs of pure $2CaO,SiO_2$ and $3CaO,P_2O_5$ are given in Table 2.

In order to ensure the closest possible approach to equilibrium, the *X*-ray analysis was pursued through successively higher temperatures, preparations heated at 1550° for 20 hr. and then annealed at 500° for 70 hr. being used as starting materials. It was realised that this procedure might incur risk of superheating if the inversions were sluggish, but there was no evidence that this occurred. The ignition for 20 hr. at 1550° made most mixes

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homogeneous, but in the region of highest liquidus temperatures there were indications of inhomogeneity in the final product. Therefore, for mixes in this region ignition at 1550° was followed by melting on the iridium wire and quenching when fully molten before annealing at 500°. Before *X*-ray analysis in the high-temperature camera all the mixes were *X*-rayed at room temperature in a focusing camera.

TABLE 2. *High-temperature camera powder measurements for intermediate polymorphs of* $2CaO,SiO_2$ *and* $3CaO,P_2O_5$.

α′-$2CaO,SiO_2$ at 1350°		β-$2CaO,SiO_2$ at 600°		α-$3CaO,P_2O_5$ at 1400°		α′-$2CaO,SiO_2$ at 1350°		β-$2CaO,SiO_2$ at 600°		α-$3CaO,P_2O_5$ at 1400°	
d	*I*	*d*	*I*	*d*	*I*	*d*	*I*	*d*	*I*	*d*	*I*
3·91	1	3·82	1	7·44	4	2·32	2	2·42	1 *	2·96	7
3·42	1	3·21	1	6·40	1	2·27	1	2·28	2	2·91	1
3·20	2	3·07	1	5·28	1	2·23	1	2·18	2	2·66	5
2·91	2	2·88	2	4·05	1	2·22	2	2·02	1	2·62	4
2·88	2	2·82	1	3·95	6			2·00	1	2·21	1
2·79	8	2·78	8	3·86	1			1·80	1	1·97	1
2·76	8	2·74	7	3·74	5					1·93	1
2·40	1	2·64	6	3·05	1						

* Broad line. Camera data and symbols as for Table 1.

In general the establishment of equilibrium below 500° required inordinately long heat treatment, and the investigation at lower temperatures was not continued.

The Figure shows that both silicocarnotite and a new phase " A " exist as homogeneous solid solutions over a range of composition that varies with temperature. Above 1450° silicocarnotite inverts without decomposition into an $\bar{\alpha}$-$3CaO,P_2O_5$ solid solution, and the previously accepted composition $5CaO,P_2O_5,SiO_2$ for silicocarnotite lies close to the composition range now determined for this phase.

Phase " A " has the approximate composition $7CaO,P_2O_5,2SiO_2$, but should not be confused with the mineral of the same composition identified by Nagelschmidt.[10] Lea and Nurse [11] obtained from a quenched preparation of $7CaO,P_2O_5,2SiO_2$ an *X*-ray pattern which they identified with nagelschmidtite, but which can now be recognised as also containing a minority of the " A " phase. After annealing this preparation they observed a change in relative intensities in the *X*-ray pattern which they ascribed to the partial formation of a low-temperature phase. The *X*-ray pattern of their annealed preparation shows it to be a mixture of the " A " phase with some unchanged nagelschmidtite. Nagelschmidtite and Trömel's phase " R " both have the structure associated with the continuous high-temperature solid-solution series α-$2CaO,SiO_2$—$\bar{\alpha}$-$3CaO,P_2O_5$, and to avoid confusion in nomenclature the term nagelschmidtite could be extended to describe the entire α-$2CaO,SiO_2$—$\bar{\alpha}$-$3CaO,P_2O_5$ solid solution range. In the region of 35% of $3CaO,P_2O_5$ these solid solutions are stable as low as 700°; in the presence of impurities the stability field may well extend to room temperature.

Although the highest-temperature form of both the end-members of the solid solution series, *i.e.*, pure α-$2CaO,SiO_2$ or pure $\bar{\alpha}$-$3CaO,P_2O_5$, do not survive quenching to room temperature, it is possible to quench the highest-temperature form of the solid solution substantially free from other phases within a very narrow region of composition at about 35% of $3CaO,P_2O_5$ in the present system; focusing-camera measurements for this material are given in Table 3. Compositions slightly richer in $2CaO,SiO_2$ yield mainly the α′-$2CaO,SiO_2$ phase after quenching, while appreciable quantities of the " A " phase are present after quenching compositions slightly richer in $3CaO,P_2O_5$. The " A " phase decomposes above 1125° into an $\bar{\alpha}$-$3CaO,P_2O_5$ solid solution richer in $2CaO,SiO_2$, and silicocarnotite. Included in Table 3 are focusing-camera measurements for the " A " phase and

[10] Nagelschmidt, *J.*, 1937, 865.
[11] Lea and Nurse, Ministry of Supply Monograph No. 11/108, 1951, p. 72.

for silicocarnotite. Below 500° there must be a region in which α′-$2CaO,SiO_2$ and "A" co-exist, which could not be determined because crystallisation rates are too slow.

The inversion from β- to α-$3CaO,P_2O_5$ at 1125° was determined from heating curves. The course of the β—α inversion curve could not be detected experimentally, but it must fall steeply with increasing $2CaO,SiO_2$ content since the mix containing 2·8% of $2CaO,SiO_2$ was stabilised in the α-form after the standard annealing at 500°. The

TABLE 3. *Room-temperature X-ray powder measurements for α̃-type, "A," and silicocarnotite phases respectively, of the compositions indicated.*

34% $3CaO,P_2O_5$ 66% $2CaO,SiO_2$		49·3% $3CaO,P_2O_5$ 30·7% $2CaO,SiO_2$		72·6% $3CaO,P_2O_5$ 27·4% $2CaO,SiO_2$		72·6% $3CaO,P_2O_5$ 27·4% $2CaO,SiO_2$	
d	*I*	*d*	*I*	*d*	*I*	*d*	*I*
3·931	5	4·26	1	8·56	2	2·37	1
3·582	3	4·04	1	7·82	1	2·29	3
3·500	3*	3·49	4	5·65	1	2·27	3
2·910	1	3·14	6	5·29	1	2·22	1
2·843	10	3·00	8	4·55	2	2·17	3
2·710	10	2·91	4	4·05	2	2·03	2
2·342	2	2·64	5	3·92	3	2·01	2
2·226	5	2·52	4	3·87	2	1·96	3
1·959	7	2·37	2	3·80	1	1·94	2*
1·912	1*	2·31	1	3·59	2	1·88	4
1·863	1*	2·29	1	3·29	3	1·87	2
1·784	4	2·23	1*	3·19	4	1·85	2
1·760	1	2·21	1	3·09	2	1·81	3
1·667	3	2·02	1	3·02	3	1·80	1
1·588	5	1·88	6†	2·96	4	1·78	2
1·563	4	1·86	4	2·82	8	1·75	4
1·489	4	1·78	3	2·80	2	1·68	1
1·431	1	1·72	1	2·72	1	1·64	1
1·420	1	1·62	1	2·60	5	1·53	3
1·352	3	1·40	1	2·58	4	1·50	2
1·267	2			2·53	2	1·45	1
1·221	2*			2·46	1		

Measurements obtained in a Guinier type focusing camera, 114 mm. diam. with Cu-K_α radiation.
* Broad line. † Doublet. Other symbols as for Table 1.

polymorphic transformation temperatures for pure $2CaO,SiO_2$ shown in the Figure are those deduced from earlier work by Welch (see Nurse [12]). The stability field for γ-$2CaO,SiO_2$ above 500° is too small to be reproduced satisfactorily, and is omitted. The stability relations between the γ-, β-, and α′-modifications of $2CaO,SiO_2$ have already been discussed by Nurse [12] and by Roy.[13]

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DEPARTMENT OF SCIENTIFIC AND INDUSTRIAL RESEARCH,
BUILDING RESEARCH STATION, WATFORD, HERTS. [*Received, October 3rd*, 1958.]

[12] Nurse, "Proc. 3rd Intern. Symposium on the Chemistry of Cement 1952," Cement and Concrete Association, London, 1954, p. 56.
[13] Roy, *J. Amer. Ceramic Soc.*, 1958, **71**, 293.

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221. *Oxidation of Polyhalogeno-compounds. Part IV.*[1] *Photochemical Oxidation and Auto-oxidation of Chlorotrifluoroethylene.*

By R. N. Haszeldine and F. Nyman.

Vapour-phase photochemical oxidation of chlorotrifluoroethylene gives chlorodifluoroacetyl fluoride in good yield. The acyl fluoride, together with a liquid peroxide, $[C_2ClF_3O]_n$, is also formed by the reaction between the liquid olefin and oxygen under autogenous pressure. Chlorotrifluoroethylene oxide is a probable by-product. Free-radical reaction schemes are postulated and correlated with earlier work on oxidation of polyhalogeno-olefins. Chlorodifluoroacetyl fluoride and oxalyl chloride fluoride were synthesised as reference compounds.

Earlier papers [1] in this series have been concerned with the photochemical or thermal oxidation of fluorine-containing polyhalogenoalkanes, and showed that under suitable conditions, *e.g.*, by the use of chlorine as initiator, suitable compounds of this type could be converted, without carbon–carbon bond cleavage, into fluoroalkanecarboxylic acids. Fluorine-containing polyhalogeno-olefins are now commercially available or readily prepared, and the controlled photochemical oxidation of such olefins without carbon–carbon cleavage offers another approach to the general problem of synthesis of fluoro-compounds containing functional groups. This paper is concerned with the photochemical oxidation and auto-oxidation of chlorotrifluoroethylene, which gives chlorodifluoroacetyl fluoride in good yield.

The photochemical oxidation of halogeno-olefins has been studied in some detail. Oxidation of tetrachloroethylene to trichloroacetyl chloride and carbonyl (di)chloride [2] is strongly inhibited by oxygen [3] and sensitised by chlorine [4] or fluorine; [5] kinetic studies [6] reveal the similarity to the chlorine-sensitised photochemical oxidation of pentachloroethane.[7] Tetrachloroethylene oxide has recently been isolated from the reaction products.[8] Photochemical chlorination of trichloroethylene is inhibited by oxygen,[9] and chlorine-initiated photochemical oxidation affords dichloroacetyl chloride.[10] Swarts [11] noted that bromofluoroethylenes readily absorbed oxygen to give acyl halides, *e.g.*,

$$CFBr{:}CFBr \longrightarrow CFBr_2{\cdot}COF; \quad CHF{:}CBr_2 \longrightarrow CHFBr{\cdot}COBr$$

Similar reactions [12,13] are:

$$CF_2Cl{\cdot}CF{:}CCl_2 \xrightarrow{O_2,\ Cl_2} CF_2Cl{\cdot}CFCl{\cdot}COCl + CF_2Cl{\cdot}CCl_2{\cdot}COCl$$

$$CF_2Cl{\cdot}CCl{:}CCl_2 \xrightarrow{O_2,\ Cl_2} CF_2Cl{\cdot}CCl_2{\cdot}COCl$$

$$CF_2Cl{\cdot}CF{:}CCl_2 \xrightarrow{O_2,\ Br_2} CF_2Cl{\cdot}CFBr{\cdot}COCl + CF_2Cl{\cdot}CFCl{\cdot}COCl$$

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[1] Francis and Haszeldine, *J.*, 1955, 6072 (Part I); Haszeldine and Nyman, *J.*, 1959, 387 (Part II); *J.*, 1959, 420 (Part III).
[2] Besson, *Compt. rend.*, 1895, **121**, 125.
[3] Leermakers and Dickinson, *J. Amer. Chem. Soc.*, 1932, **54**, 4648.
[4] Dickinson and Leermakers, *ibid.*, p. 3852; Dickinson and Carrico, *ibid.*, 1934, **56**, 1473.
[5] Miller and Dittman, *ibid.*, 1956, **78**, 2793.
[6] Schott and Schumacher, *Z. phys. Chem.*, 1941, *B*, **49**, 107.
[7] Schumacher and Thürauf, *ibid.*, 1941, *A*, **189**, 183.
[8] Kirkbride, U.S.P. 2,321,823 (1943); *Chem. Abs.*, 1943, **37**, 6676; Frenkel, Johnson, and Pitt, *J. Org. Chem.*, 1957, **22**, 1119.
[9] Müller and Schumacher, *Z. phys. Chem.*, 1937, *B*, **35**, 455.
[10] *Idem, ibid.*, 1937, *B*, **37**, 365.
[11] Swarts, *Bull. Acad. roy. Belg.*, 1897, **33**, 439; 1897, **34**, 307; 1897, **35**, 849; 1898, **36**, 532; *Rec. Trav. chim.*, 1898, **17**, 321; McBee, Pierce, and Christman, *J. Amer. Chem. Soc.*, 1955, **77**, 1851.
[12] Chaney, U.S.P. 2,439,505/1948; *Chem. Abs.*, 1948, **42**, 7315; U.S.P. 2,456,768/1948; *Chem. Abs.*, 1949, **43**, 4683; U.S.P. 2,514,473/1950; *Chem. Abs.*, 1950, **44**, 9474.
[13] Henne and Fox, *J. Amer. Chem. Soc.*, 1954, **76**, 479.

The reaction between liquid chlorotrifluoroethylene and molecular oxygen has been investigated by Myers [14] whose results do not agree with those obtained in the present work; whilst this was in progress a patent was issued on the subject,[15] but the yields, etc., there claimed differ appreciably from our own.

Chlorotrifluoroethylene and oxygen react together only very slowly in the vapour phase in the absence of light; 85% of the olefin is recovered after six months, and chlorodifluoroacetyl fluoride is the only product. In the presence of water this vapour-phase reaction is even slower. The reaction is greatly accelerated by ultraviolet light, the major product being chlorodifluoroacetyl fluoride ($CF_2{:}CFCl \longrightarrow CF_2Cl{\cdot}COF$; 77% yield, 47% conversion of olefin after 5 days) together with smaller amounts of breakdown products such as carbonyl difluoride, carbon dioxide, and silicon tetrafluoride. Chlorodifluoroacetyl fluoride is itself slowly oxidised photochemically to carbon dioxide and carbonyl difluoride (together with silicon tetrafluoride). Photolysis of the acyl fluoride in absence of oxygen gives 1 : 2-dichlorotetrafluoroethane, dichlorodifluoromethane, carbonyl difluoride, and carbonyl chloride fluoride; chlorotrifluoromethane was not detected:

$$CF_2Cl{\cdot}COF \xrightarrow{h\nu} \dot{C}F_2Cl \xrightarrow{CF_2Cl{\cdot}COF} CF_2Cl_2$$
$$\dot{C}F_2Cl \longrightarrow (CF_2Cl)_2$$

Dichloro-tetrafluoroethane or -difluoromethane was not formed during photochemical oxidation of chlorotrifluoroethylene. The chlorodifluoroacetyl fluoride so obtained is spectroscopically identical with a sample prepared as follows:

$$CF_2Cl{\cdot}CO_2Na \xrightarrow{PCl_5} CF_2Cl{\cdot}COCl \xrightarrow{KF} CF_2Cl{\cdot}COF$$

The identified products of the photochemical oxidation of chlorotrifluoroethylene account for virtually all the olefin consumed; nevertheless, examination was made for two other products that could conceivably be formed without carbon–carbon fission, *i.e.*, oxalyl chloride fluoride and oxalyl difluoride. Oxalyl chloride fluoride has a characteristic absorption spectrum with double carbonyl absorption. Attempts to convert oxalyl dichloride or chloride fluoride into oxalyl difluoride failed, since only breakdown occurred under more forcing conditions. However, the absence of a double carbonyl peak from the infrared spectrum of the more volatile photolysis products of chlorotrifluoroethylene shows that oxalyl chloride fluoride or difluoride is absent, or present to only a very small extent.

The halogen-sensitised photochemical oxidation of chlorotrifluoroethylene was next investigated. Addition of even small quantities of chlorine, *e.g.*, a molar ratio of olefin to chlorine of *ca.* 200 : 1, caused spontaneous pyrolysis at low temperature when liquid olefin was still present. The introduction of bromine into vapour-phase mixtures of the olefin and oxygen resulted in an immediate explosion. The sensitivity of the reaction between chlorotrifluoroethylene and oxygen towards sources of free radicals is clearly demonstrated.

Myers [14] stated that in the absence of liquid olefin the reaction between chlorotrifluoroethylene and oxygen is immeasurably slow, and in general this agrees with our results. From the reaction of the liquid olefin and oxygen he obtained a product of b. p. *ca.* 15° higher than that of the olefin (b. p. −26·8°) and postulated that this was the peroxide $\overline{CF_2{\cdot}CFCl{\cdot}O{\cdot}O}$. Products of higher b. p. were not obtained. Myers discounted the possibility of chlorodifluoroacetyl fluoride, since hydrolysis gave oxalate, fluoride, and chloride ions in the ratio 1 : 3 : 1, and chlorodifluoroacetic acid is known to be stable in aqueous solution; it should be noted, however, that the acid will break down if heated with concentrated aqueous alkali. Our own investigation of the reaction between liquid chlorotrifluoroethylene and oxygen shows that one mole of olefin reacts with only ½ mole

[14] Myers, *Ind. Eng. Chem.*, 1953, **45**, 1783.
[15] Hurka, U.S.P. 2,676,983/1954; *Chem. Abs.*, 1955, **49**, 5510.

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of oxygen in accord with the stoicheiometry, $CF_2{:}CFCl + \frac{1}{2}O_2 \longrightarrow CF_2Cl{\cdot}COF$; Myers found the oxygen uptake to be equimolar. The products are chlorodifluoroacetyl fluoride and the volatile breakdown materials mentioned earlier, but in addition a relatively involatile liquid, not hitherto reported, was isolated. This detonated when warmed and had other peroxidic properties. Its yield decreases with reaction time in favour of increased formation of chlorodifluoroacetyl fluoride. The analytical data give the formula $(C_2ClF_3O)_n$ and show that the oxygen is peroxidic with one O–O link per two C_2ClF_3O units. Hydrolysis affords chlorodifluoroacetic and oxalic acid together with carbon dioxide, chloride, and fluoride.

An attempt was made to detect the formation of the epoxide $\overline{CF_2{\cdot}CFCl{\cdot}O}$ during the oxidation of chlorotrifluoroethylene. When oxygen was bubbled into refluxing liquid chlorotrifluoroethylene at atmospheric pressure, chlorodifluoroacetyl fluoride and an unstable compound characterised by a strong band at 6·4 μ in its infrared spectrum were formed. Complete separation of this new compound from chlorodifluoroacetyl fluoride could not be effected even when the excess of olefin was removed by rapid treatment with chlorine, but analysis of the mixture indicated that it is an isomer of chlorodifluoroacetyl fluoride, but not trifluoroacetyl chloride, and is thus probably chlorotrifluoroethylene oxide. This is presumably the unknown compound noted by Myers; its hydrolysis to oxalic acid is as expected:

$$CF_2\!-\!CFCl + H_2O \longrightarrow CF_2(OH){\cdot}CFCl{\cdot}OH \xrightarrow{H_2O} (CO_2H)_2 + 3F^- + Cl^-$$

Discussion.—It is suggested that chlorotrifluoroethylene and oxygen react slowly, even in the dark, to give a cyclic peroxide as an unstable intermediate:

$$CF_2{:}CFCl + O_2 \longrightarrow \dot{C}FCl{\cdot}CF_2{\cdot}O{\cdot}O{\cdot} \xrightarrow{CF_2{:}CFCl} \begin{matrix} CFCl{\cdot}CF_2{\cdot}O \\ | \\ CFCl{\cdot}CF_2{\cdot}O \end{matrix}$$

Attack of oxygen on the CF_2 group of chlorotrifluoroethylene is followed, in the liquid phase, by attack on a second molecule of the olefin to give the relatively involatile peroxide $[C_2ClF_3O]_2$. This satisfies the analytical data for the explosive liquid $[C_2ClF_3O]_n$, with one peroxy-group per two molecules of olefin, isolated from the reaction of liquid chlorotrifluoroethylene with oxygen. A linear structure for $[C_2F_3ClO]_n$ must be discounted, since it would be a chlorofluoroalkyl ether, not a peroxide, and chemically and thermally would be much more stable. The peroxide could then function as a source of free radicals on exposure to light, or as a source of chlorotrifluoroethylene oxide.

The photochemical oxidation of chlorotrifluoroethylene was carried out in Pyrex vessels so that the wavelength of the initiating radiation is >3000 Å. A peroxide would absorb light of wavelength > 3000 Å and its photolysis would give rise to a free radical capable of initiating the photochemical oxidation chain reaction. The decrease in the rate of the dark reaction in presence of water can be attributed to removal of the peroxide by hydrolysis. The ability of chlorotrifluoroethylene, after " activation " by being kept with small amounts of oxygen, to oxidise fresh olefin can also be accounted for by peroxide formation.

Chlorine atoms are the chain carriers in the free-radical chain reaction which sets in after initiation by a free radical R [*e.g.*, $(CFCl{\cdot}CF_2{\cdot}O{\cdot})_2$] acting in the same manner as a chlorine atom in the following sequence:

Chain reaction:

$$Cl{\cdot} + CF_2{:}CFCl \longrightarrow CF_2Cl{\cdot}CFCl{\cdot} \xrightarrow{O_2} CF_2Cl{\cdot}CFCl{\cdot}O_2{\cdot}$$

$$CF_2Cl{\cdot}CFCl{\cdot}O_2{\cdot} \xrightarrow{Cl_2} CF_2Cl{\cdot}CFCl{\cdot}O_2Cl \xrightarrow{h\nu} CF_2Cl{\cdot}CFCl{\cdot}O{\cdot} + {\cdot}OCl$$

$$2{\cdot}OCl \longrightarrow O_2 + Cl_2$$

$$CF_2Cl{\cdot}CFCl{\cdot}O{\cdot} \longrightarrow CF_2Cl{\cdot}COF + Cl{\cdot} \longrightarrow \text{etc.}$$

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The sensitivity of mixtures of chlorotrifluoroethylene and oxygen to small quantities of chlorine or bromine indicates long reaction chains. That atom or radical attack is exclusively on the CF_2 group of chlorotrifluoroethylene has already been established.[16] The formation of the $CF_2Cl{\cdot}CFCl{\cdot}O_2{\cdot}$ radical, its conversion into the perhalogenoalkoxy-radical $CF_2Cl{\cdot}CFCl{\cdot}O{\cdot}$ with chlorine on the α-carbon atom, and loss of this chlorine as an atom, are steps analogous to those proposed for the photochemical oxidation of chlorofluoroethanes to trifluoroacetyl chloride.[1]

Chlorodifluoroacetyl fluoride could also be formed *via* rearrangement of chlorotrifluoroethylene oxide:

$$CF_2Cl{\cdot}CFCl{\cdot}O_2{\cdot} \longrightarrow CF_2\!-\!CFCl + {\cdot}OCl$$
$$\qquad\qquad\quad O$$

$$CF_2Cl{\cdot}CFCl{\cdot}O{\cdot} \longrightarrow CF_2\!-\!CFCl + Cl{\cdot}$$
$$\qquad\qquad\quad O$$

$$CF_2\!-\!CFCl \longrightarrow CF_2Cl{\cdot}COF$$
$$O$$

Support for the postulate that the chlorine atom is the chain carrier in the above reactions comes from consideration of the products from other unsymmetrical polyhalogeno-olefins. Thus, a similar reaction scheme can be formulated for the bromofluoroethylenes with bromine atom as carrier, and for trichloroethylene:

$$Br{\cdot} + CFX{:}CBr_2 \longrightarrow CFXBr{\cdot}CBr_2{\cdot} \xrightarrow{O_2} CFXBr{\cdot}COBr \quad (X = H \text{ or } Br)$$

$$Cl{\cdot} + CHCl{:}CCl_2 \longrightarrow CHCl_2{\cdot}CCl_2{\cdot} \xrightarrow{O_2} CHCl_2{\cdot}COCl$$

The direction of free-radical or atom attack on these olefins is either established [17] or can be predicted with certainty from recent work on the direction of addition of a free radical to unsymmetrical olefins.[18] Similarly, Chaney's [12] and Henne and Fox's [13] results can be reinterpreted as:

$$X{\cdot} + CF_2Cl{\cdot}CF{:}CCl_2 \longrightarrow CF_2Cl{\cdot}CFX{\cdot}CCl_2{\cdot}$$

$$CF_2Cl{\cdot}CFX{\cdot}CCl_2{\cdot} \xrightarrow{O_2} CF_2Cl{\cdot}CFX{\cdot}CCl_2{\cdot}O{\cdot} \longrightarrow Cl{\cdot} + CF_2Cl{\cdot}CFX{\cdot}COCl$$
(where X = Cl or Br)

The direction of radical or atom addition to an olefin of the type $CZ_3{\cdot}CF{:}CCl_2$ (where Z = halogen) can be predicted with certainty to be to the CF group.[17] There is thus no need to postulate halogen-atom attack on the epoxide $CF_2Cl{\cdot}\overbrace{CF{\cdot}CCl_2{\cdot}O}$, and it is noteworthy that Henne and Fox cited no evidence for the formation of an epoxide.

Experimental

General techniques were described in Parts I—III. Reactants and products were measured, purified, etc., in an apparatus for manipulation of volatile compounds, *in vacuo*. The reactants could thus be freed from traces of air or other impurities and, since reactions were carried out in sealed Pyrex or Dreadnought tubes filled directly from the vacuum-apparatus and sealed *in vacuo*, there was no danger that unwanted catalysts, moisture, etc., could become incorporated. Products were identified by b. p., vapour pressure, molecular weight, infrared spectroscopy, analysis, etc. Spectroscopically pure chlorotrifluoroethylene was redistilled, and a middle cut degassed by repeated freezing and thawing, then redistilled several times. Tests for peroxides were negative. A Hanovia S. 250 ultraviolet lamp was used without the Wood's filter at 5—15 cm. from the reaction vessel. Typical experiments are reported below.

[16] Haszeldine and Steele, *J.*, 1953, 1592; 1954, 3747.
[17] Kharasch, Norton, and Mayo, *J. Org. Chem.*, 1939, **3**, 48; Haszeldine and Liptrot, unpublished results.
[18] See, *e.g.*, Cadogan and Hey, *Quart. Rev.*, 1954, **8**, 308; Haszeldine, *J.*, 1952, 2504 *et seq.*

The Vapour-phase Dark Reaction.—Chlorotrifluoroethylene (0·381 g., 3·27 mmoles) and oxygen (0·111 g., 3·47 mmoles) were sealed in a 50-ml. Pyrex tube (initial pressure *ca.* 3·2 atm.) and kept in darkness for *ca.* 6 months. The volatile products were distilled *in vacuo* to give unchanged chlorotrifluoroethylene (0·324 g., 2·78 mmoles, 85%) and chlorodifluoroacetyl fluoride (0·065 g., 0·49 mmole, 100% based on olefin used), shown spectroscopically to be the only product and identified by comparison of its infrared spectrum with that of a known sample.

The Vapour-phase Dark Reaction in the Presence of Water.—Chlorotrifluoroethylene (0·348 g., 2·99 mmoles), water (3·0 ml.), and oxygen (0·098 g., 3·06 mmoles), sealed in a 50-ml. Pyrex tube (initial pressure *ca.* 2·9 atm.) and kept in darkness for *ca.* 6 months, gave only unchanged chlorotrifluoroethylene (0·335 g., 2·88 mmoles, 96%).

Photochemical Oxidation.—Chlorotrifluoroethylene (1·270 g., 10·9 mmoles) and oxygen (0·308 g., 9·63 mmoles) were sealed in a 75-ml. Pyrex tube (initial pressure *ca.* 7·0 atm.) and exposed to ultraviolet light for 126 hr. The volatile products were distilled to give: (*a*) an unidentified residue (*ca.* 0·1 g.); (*b*) a fraction shown spectroscopically to consist of chlorotrifluoroethylene (0·429 g., 5·00 mmoles, 53% recovery) and chlorodifluoroacetyl fluoride (0·520 g., 3·93 mmoles, 77% yield), and (*c*) a mixture (0·165 g., 2·43 mmoles) of carbon dioxide, silicon tetrafluoride, and carbonyl difluoride. Shorter irradiation times with lower conversions or longer irradiation times with higher conversions of olefin failed to give significantly higher yields of the acyl fluoride.

Fractions (*b*) from several such tubes were combined and refractionated several times *in vacuo* to give pure chlorodifluoroacetyl fluoride (Found: *M*, 133. Calc. for C_2ClF_3O: *M*, 132·5), spectroscopically identical with a known sample. Further proof of structure was obtained by treating a sample (0·402 g.) with water (1·0 ml.) in a sealed tube for 1 hr. The aqueous solution was treated with an excess of silver carbonate, filtered, and freeze-dried. The residue was extracted with ether, and the ethereal extract evaporated *in vacuo* to give silver chlorodifluoroacetate, spectroscopically identical with a sample prepared directly from chlorodifluoroacetic acid.

Initiation by Activated Olefin.—Chlorotrifluoroethylene (0·735 g., 6·30 mmoles), which had been kept with oxygen (*ca.* 10%) for two weeks, was sealed with oxygen (0·256 g., 8·00 mmoles) in a 100-ml. Pyrex tube (initial pressure *ca.* 3·7 atm.) and exposed to ultraviolet light for 70 min. The products were distilled *in vacuo* to give: (*a*) an unidentified residue (*ca.* 0·1 g.), (*b*) a fraction shown spectroscopically to consist of chlorotrifluoroethylene (0·079 g., 0·68 mmole, 11% recovery) and chlorodifluoroacetyl fluoride (0·445 g., 3·36 mmoles, 60% yield), and (*c*) a mixture (0·108 g., 1·44 mmoles) of carbon dioxide, silicon tetrafluoride, carbonyl difluoride, and carbonyl chloride fluoride.

Chlorine-sensitised Oxidation.—Chlorotrifluoroethylene (0·761 g., 6·52 mmoles), chlorine (0·002 g., 0·028 mmole), and oxygen (0·301 g., 9·40 mmoles) were sealed in a 70-ml. Pyrex tube. When the mixture reached *ca.* −30° in subdued daylight a luminous flame-front traversed the tube; a second appeared 15 sec. later, and carbon was deposited on each occasion. Fractionation *in vacuo* of the products from several such reactions gave chlorotrifluoroethylene, chlorodifluoroacetyl fluoride, 1 : 1 : 2-trichlorotrifluoroethane, and the breakdown products reported above.

Bromine-sensitised Oxidation.—Chlorotrifluoroethylene (0·757 g., 6·50 mmoles) and oxygen (0·308 g., 9·60 mmoles) were sealed in a 50-ml. Pyrex tube together with a fragile ampoule containing bromine (0·067 g., 0·42 mmole). When the temperature had reached that of the room the ampoule was broken to release the bromine; the tube immediately exploded.

Liquid-phase Auto-oxidation.—The results of a series of dark experiments carried out in thick-walled Dreadnought tubes of 18 ml. capacity are summarised in the annexed Table.

CF_2:CFCl	O_2 (mmole)	H_2O	Initial press. (atm.)	(Time (hr.)	CF_2:CFCl (% recovery)	Products $CO_2 + SiF_4 +$ $COF_2 + COFCl$ (mmole)	CF_2Cl·COF (mmole)	Yield (%)	Peroxide (g.)
12·4	14·2	0	25	1·0	97	0·50	0	0	0
8·66	12·2	3·68	24	1·0	92	0·45[a]	0	0	0
4·36	9·20	0	18	12·5	16	0·33	1·19	33	0·240
4·87	9·50	0	19	24	18	0·66	2·13	53	0·150
3·69	3·70[b]	0	12	48	0	0·31[c]	2·29	62	0·160

[a] CO_2 only. [b] 40% of oxygen unchanged at end of expt. [c] COF_2 only.

In an experiment at atmospheric pressure, chlorotrifluoroethylene (10 g.) was placed in the still-pot of a small low-temperature distillation column, the condenser of which was cooled with an alcohol–solid carbon dioxide slurry. Oxygen was bubbled into the refluxing liquid for 24 hr. The products, other than a small liquid residue (0·4 g.), were volatile. These were distilled *in vacuo* to give a number of arbitrary fractions. Infrared spectroscopic examination of the last of these (0·62 g.) showed the presence of an unknown compound characterised by a strong absorption band at 6·4 μ, as well as unchanged olefin and chlorodifluoroacetyl fluoride. This fraction was treated rapidly with chlorine (0·1 g.) in order to remove the olefin as 1 : 1 : 2-trichlorotrifluoroethane by distillation *in vacuo*. Infrared spectroscopic examination of the remaining material showed that it contained chlorodifluoroacetyl fluoride and the unknown compound (Found for the mixture: C, 17·3%; *M*, 130. Calc. for C_2OClF_3: C, 18·1%; *M*, 132·5).

Chlorotrifluoroethylene Peroxide.—This was a product of the reaction of liquid chlorotrifluoroethylene with oxygen as described above. The *peroxide* is a clear, colourless liquid of vapour pressure *ca.* 3 mm. at 20°, which decomposes in moist air and detonates violently on heating [Found: C, 17·3; Cl, 26·5; F, 41·2%; iodine equiv., 0·54. $(C_2ClF_3O)_n$ requires C, 18·1; Cl, 26·8; F, 43·0%; iodine equiv., 0·50]. The peroxide was analysed for chlorine and fluorine by fusion of a sample with sodium at 600° for 2 hr. in a Parr bomb. Chloride was then determined gravimetrically as silver chloride, and fluoride as fluorosilicic acid by titration with thorium nitrate solution.

Iodine was liberated when the peroxide was treated with aqueous potassium iodide, but the predominant reaction was that of hydrolysis, and hence the usual methods for determining the oxidising power of peroxides could not be used. The method ultimately employed was based on a procedure described by Nosaki.[19] A weighed sample (*ca.* 0·2 g.) was added to 30 ml. of a solution of sodium iodide in acetic anhydride, whereupon iodine was liberated immediately. After 15 min., 50 ml. of distilled water were added and the iodine was determined by titration with standard sodium thiosulphate.

The peroxide was rapidly and exothermically hydrolysed by water, and attack on the glass vessel produced sodium fluorosilicate. Hydrolysis with water in a sealed tube gave Cl^-, 15·7%, and C as CO_2, 8·6%. The aqueous solution was also treated with an excess of silver carbonate, filtered, and freeze-dried. The residue was extracted with ether, and the ether evaporated *in vacuo* to give a mixture of sodium and silver chlorodifluoroacetates and sodium oxalate, all identified spectroscopically. The sodium arose from attack on the glass vessel by the hydrofluoric acid formed in the hydrolysis. The peroxide thus hydrolyses with approx. 50% breakdown to chloride, fluoride, and carbonate [Calc. for $(C_2ClF_3O)_{2n} \xrightarrow{H_2O} 2nCO_2 + nCl^-$: Cl^-, 13·4%; C as CO_2, 9·0%], and approx. 50% conversion, probably *via* chlorotrifluoroethylene oxide and chlorodifluoroacetyl fluoride, into chlorodifluoroacetic acid, oxalic acid, chloride, and fluoride.

Synthesis of Chlorodifluoroacetyl Fluoride.—Sodium chlorodifluoroacetate (5·2 g.) and phosphorus pentachloride (10·0 g.) were thoroughly mixed and heated to 100° under reflux. The volatile products were condensed in a liquid oxygen-cooled trap connected to the top of the condenser, then distilled *in vacuo* to give chlorodifluoroacetyl chloride (2·4 g., 47%) (Found: *M*, 150. Calc. for $C_2Cl_2F_2O$: *M*, 149), b. p. 24° (isoteniscope). Chlorodifluoroacetyl chloride (0·899 g.) and dry potassium fluoride (10 g.) were sealed in a 200-ml. Pyrex tube and kept at 100° for 36 hr. The volatile products were distilled *in vacuo* to give *chlorodifluoroacetyl fluoride* (0·52 g., 65%) (Found: C, 17·8%; *M*, 132·5. C_2ClF_3O requires C, 18·1%; *M*, 132·5), b. p. −17·5° (isoteniscope), and trifluoroacetyl fluoride (0·19 g.), identified spectroscopically.

The structure of the chlorodifluoroacetyl fluoride (easily distinguished from its isomer trifluoroacetyl chloride by infrared spectroscopy) was confirmed as follows. The acyl halide (0·334 g.) and water (1·0 ml.) were shaken together in a sealed tube for 1 hr., and the aqueous solution was then treated with an excess of silver carbonate, filtered, and freeze-dried. The residue was extracted with ether, and the ethereal extract evaporated *in vacuo* to give silver chlorodifluoroacetate (0·542 g., 91%), spectroscopically identical with a sample prepared directly from chlorodifluoroacetic acid.

Swarts [20] reported b. p. 34° for chlorodifluoroacetyl chloride prepared by chlorination of

[19] Nosaki, *Analyt. Chem.*, 1946, **18**, 583.
[20] Swarts, *Bull. Acad. roy. Belg.*, 1907, 339

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2 : 2-difluoroethanol; the acyl chloride obtained recently [21] by pyrolysis of *sym*-dichlorotetrafluoroacetone at 500—750° had b. p. 24·8°.

Carbonyl absorption is shown as follows: $CF_2Cl{\cdot}COCl$, 5·47 μ; $CF_3{\cdot}COCl$, 5·40 μ; $CF_2Cl{\cdot}COF$, 5·30 μ; $CF_3{\cdot}COF$, 5·23 μ; $CF_2Cl{\cdot}CO_2Ag$, 6·01 μ.

Photolysis of Chlorodifluoroacetyl Fluoride.—Chlorodifluoroacetyl fluoride (0·394 g., 2·97 mmoles) was sealed in a 320-ml. silica tube and exposed to ultraviolet light for 24 hr. The volatile products were distilled *in vacuo* to give a mixture of chlorodifluoroacetyl fluoride (0·261 g., 1·97 mmoles, 66% recovery) and 1 : 2-dichlorotetrafluoroethane, and a fraction, separated by treatment with aqueous base, consisting of dichlorodifluoromethane (0·015 g., 0·12 mmole, 8%) and a mixture (0·042 g., 0·60 mmole) of carbonyl difluoride, carbonyl chloride fluoride, and a trace of silicon tetrafluoride.

Photochemical Oxidation of Chlorodifluoroacetyl Fluoride.—The acyl fluoride (0·402 g., 3·03 mmoles) and oxygen (0·308 g., 9·6 mmoles) were sealed in a 300-ml. silica tube (initial pressure *ca.* 1·0 atm.) and irradiated for 30 hr. The volatile products were shaken with mercury to remove chlorine and distilled *in vacuo* to give chlorodifluoroacetyl fluoride (0·050 g., 0·38 mmole, 12%) and a mixture (0·347 g., 5·56 mmoles) of carbon dioxide, silicon tetrafluoride, carbonyl difluoride, and a small amount of dichlorodifluoromethane.

Oxalyl Chloride Fluoride.—Oxalyl dichloride (2·15 g., 16·9 mmoles) and anhydrous potassium fluoride (10 g.) were sealed in a 200-ml. Pyrex tube and kept at 100° for 24 hr. The volatile products were (*a*) oxalyl dichloride (1·60 g., 12·6 mmoles, 75%), (*b*) *oxalyl chloride fluoride* (0·231 g., 2·09 mmoles, 49% yield based on oxalyl dichloride used) (Found: C, 21·4%; *M*, 110·5. C_2ClFO_2 requires C, 21·7 %; *M*, 110·5), b. p. −21°/140 mm., and (*c*) a mixture (0·080 g., 1·33 mmoles) of carbon dioxide and silicon tetrafluoride. Oxalyl chloride fluoride has characteristic double carbonyl absorption at 5·36, 5·58 μ; cf. $(COCl)_2$ 5·36, 5·8 μ.

Attempted Synthesis of Oxalyl Difluoride.—The dropwise addition of oxalyl dichloride to freshly sublimed antimony trifluoride (alone or with 10 moles % of antimony pentachloride added) at room temperature gave only a mixture of carbon dioxide and carbonyl chloride fluoride.

Reaction of oxalyl dichloride with anhydrous potassium fluoride in sealed tubes at temperatures between 100° and 150° for periods varying between 3 and 24 hr. gave only oxalyl dichloride, oxalyl chloride fluoride, and breakdown products.

Infrared Spectra.—These were determined on a Perkin–Elmer Model 21 Spectrophotometer with sodium chloride optics:

$CF_2Cl{\cdot}COCl$ (vapour): 2·87 (w), 5·30 (m), 5·47 (s), 5·80 (m), 7·38 (w), 8·47 (vs), 9·83 (vs), 11·63 (vs), 12·53 (s), 14·51, 14·60, 14·68 μ (m triplet). Here and below, s = strong, w = weak vs = very strong, m = medium strength.

$CF_2Cl{\cdot}COF$ (vapour): 2·68 (w), 5·30 (s), 7·88 (s), 8·40 (vs), 9·05 (vs), 10·25, 10·35 (vs doublet), 11·59 (w), 12·94, 13·03, 13·15 (s triplet), 14·30, 14·49, 14·60 μ (s triplet).

$CF_2Cl{\cdot}CO_2Ag$ (Nujol mull): 3·30 (w), 6·00, 6·15 (s doublet), 6·80 (w), 7·07 7·13 (s doublet), 7·65 (w), 7·95 (m), 8·67 (s), 10·42, 10·51 (s doublet) 12·20 (s), 13·70 (s).

$COF{\cdot}COCl$ (vapour): 2·71 2·82 (w doublet), 4·69 (w), 4·83, 4·87 (w doublet), 5·36 (vs), 5·58 (vs), 7·10 (w), 8·36 (vs), 9·67 (s), 10·65, 10·70 (vs doublet), 12·83 (vs), 14·00 (vs).

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UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, October 2nd*, 1958.]

[21] Miller and Woolf, U.S.P. 2,741,634/1956.

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222. *The Stability Constants of the Silver Complexes of Some Aliphatic Amines and Amino-acids.*

By S. P. Datta and A. K. Grzybowski.

The stability constants of the silver complexes of 2-aminoethanol (ethanolamine), 2-aminoethyl phosphate, 2-aminoethyl sulphate, taurine, 2-amino-2-methylpropane-1 : 3-diol, sarcosine, and *NN*-dimethylglycine have been determined electrometrically at 25°, and for glycine and arginine over a wide temperature range. The thermodynamic quantities associated with the formation of the glycine and arginine silver complexes have been calculated, and their significance discussed.

During recent years a number of accurate determinations, over a wide temperature range, have been made in this laboratory of the acid dissociation constants of a number of aliphatic amines and amino-acids.[1] These determinations were made from e.m.f. measurements of cells without liquid junction containing hydrogen and silver–silver chloride electrodes and amine–chloride buffer solutions. In such cells there may be interactions between the silver chloride of the electrodes and the basic form of the amino-groups of the buffer acids. It was therefore necessary to know the stability constants of the silver complexes of these compounds in order to apply corrections to the e.m.f. results when necessary.

For most of the compounds determinations were made only at 25°, but with both arginine and glycine a wide temperature range was covered. The stability constants were determined from glass-electrode pH measurements during the titration with alkali of the acid form of the amine in the presence of silver nitrate. The values of the constants for glycine at 25° were determined by means of Irving and Rossotti's equation:[2]

$$\frac{\bar{n}}{(\bar{n}-1)[\mathrm{L}]} = \frac{(2-\bar{n})[\mathrm{L}]}{(\bar{n}-1)} K_1K_2 - K_1 \quad . \quad . \quad . \quad . \quad . \quad (1)$$

All the others were determined from Rossotti and Rossotti's equation:[3]

$$[\mathrm{L}]^2\left(\frac{2}{\bar{n}}-1\right) = \frac{1}{K_2}[\mathrm{L}]\left(1-\frac{1}{\bar{n}}\right) + \frac{1}{K_1K_2} \quad . \quad . \quad . \quad . \quad (2)$$

where [L] is the ligand concentration, $\bar{n}$ is the average number of ligand molecules bound per silver atom, and the successive stability constants are: $K_1 = [\mathrm{LAg}]/[\mathrm{L}][\mathrm{Ag}^+]$ and $K_2 = [\mathrm{L_2Ag}]/[\mathrm{L}][\mathrm{LAg}]$. In all cases the term ligand refers to that form of the compound where the amino-group is unprotonated.

The hydrogen-ion concentration was calculated from the experimentally determined pH values by using the relation, $[\mathrm{H}^+] = \text{antilog}\,[-\mathrm{pH} - \log \gamma_{\mathrm{H}^+}]$, where γ_{H^+} was assumed to be equal to $\gamma_{\pm(\mathrm{HCl})}$ at the average ionic strength during the titration.

The constants of equations (1) or (2) were determined for glycine, arginine, and 2-amino-2-methylpropane-1 : 3-diol by the method of least squares after the linearity of the points used had been determined graphically. The graphical method only was used for the other ligands. The values of $\gamma_{\pm(\mathrm{HCl})}$ used were those of Bates and Bower;[4] the acid dissociation constants of the ligand amino-groups were determined from titration curves or calculated from the thermodynamic constants.

It was possible that silver ions might interact with the phosphate radical of 2-aminoethyl phosphate. That this is not so was established by a comparison of the titration

[1] Datta and Grzybowski, *Trans. Faraday Soc.*, 1958, **54**, 1179.
[2] Irving and Rossotti, *J.*, 1953, 3397.
[3] Rossotti and Rossotti, *Acta Chem. Scand.*, 1955, **9**, 1166.
[4] Bates and Bower, *J. Res. Nat. Bur. Stand.*, 1954, **53**, 283.

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curves for this compound in the absence and in the presence of silver ions, the shapes of these curves indicating that the silver ions were only complexed by the basic form of the amino-group.

Results and Discussion.—The values of the stability constants obtained are shown in Tables 1 and 2. The values of log K_1 and log K_2 for the arginine and glycine complexes at different temperatures were fitted to Harned and Robinson's equation:[5]

$$\log K = A/T - D + CT \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

The values of the constants thus obtained are shown in Table 3.

TABLE 1. *Concentration stability constants at 25° of the silver complexes of some aliphatic amines and amino-acids.*

(Ligand refers to that ionic form of the compound in which the amino-group is not protonated.)

Ligand	Amino pK_a'	log K_1	log K_2	Mean I	Observed range of $\bar{n}$	Ligand : metal ratio	No. of points on titration curve
2-Aminoethanol	$9{\cdot}51_4$	$3{\cdot}29_3$	$3{\cdot}53_4$	$0{\cdot}015_2$	0—1·5	4	15
2-Aminoethyl phosphate...	$10{\cdot}31_6$	$3{\cdot}89_3$	$3{\cdot}22_8$	$0{\cdot}034_6$	0—1·4	4	16
2-Aminoethyl phosphate...	$10{\cdot}34_2$	$3{\cdot}87_9$	$3{\cdot}25_3$	$0{\cdot}026_6$	0—1·76	6	12
2-Aminoethyl sulphate ...	$9{\cdot}13_5$	$3{\cdot}42_8$	$3{\cdot}48_0$	$0{\cdot}013_6$	0·2—1·7	4	18
Taurine	$8{\cdot}95_0$	$3{\cdot}19_4$	$3{\cdot}19_9$	$0{\cdot}014_1$	0—1·5	4	13
2-Amino-2-methylpropane-1 : 3-diol.....	$8{\cdot}79_9$	$3{\cdot}20_0$	$3{\cdot}66_2$	$0{\cdot}027_5$	0·2—1·2	2	27
Sarcosine	$10{\cdot}11_0$	$3{\cdot}04_2$	$2{\cdot}84_9$	$0{\cdot}016_5$	0·2—1·0	4	11
NN-Dimethylglycine	$9{\cdot}86_8$	$2{\cdot}91_0$	$2{\cdot}81_8$	$0{\cdot}013_2$	0·4—0·9	4	7

TABLE 2. *Concentration stability constants of the silver complexes of glycine and arginine.*

[The values of log $K_{calc.}$ were derived from the parameters of equation (3) given in Table 3.]
Δ = log $K_{calc.}$ − log $K_{obs.}$ σ = Standard error.

Temp.	Amino-pK_a'	log $K_{1obs.}$	log $K_{1calc.}$	$10^3\Delta$	log $K_{2obs.}$	log $K_{2calc.}$	$10^3\Delta$	Observed range of $\bar{n}$	Ligand : metal ratio	No. of points on titration curve
				Glycine. Mean I = 0·01.						
5°	$10{\cdot}26_4$	$3{\cdot}47_6$	$3{\cdot}47_2$	+2	$3{\cdot}87_6$	$3{\cdot}85_3$	−17	0—1·8	3	20
15	$9{\cdot}96_8$	$3{\cdot}48_2$	$3{\cdot}48_4$	+1	$3{\cdot}63_4$	$3{\cdot}63_6$	+2	0—1·8	3	18
25	9·66	$3{\cdot}44_5$	$3{\cdot}43_1$	−14	$3{\cdot}37_2$	$3{\cdot}43_2$	+60	0—1·3	2	17
35	$9{\cdot}44_5$	$3{\cdot}29_9$	$3{\cdot}32_1$	+22	$3{\cdot}26_7$	$3{\cdot}23_9$	−28	0—1·5	3	16
45	$9{\cdot}21_4$	$3{\cdot}16_9$	$3{\cdot}15_7$	−12	$3{\cdot}10_1$	$3{\cdot}05_7$	−44	0—1·7	3	22
55	$8{\cdot}98_2$	$2{\cdot}94_4$	$2{\cdot}94_6$	+2	$2{\cdot}85_5$	$2{\cdot}88_3$	+28	0—1·3	3	16
σ5°, 55°			$0{\cdot}01_5$			$0{\cdot}04_5$				
σ25°			0·01			$0{\cdot}03_0$				
				Arginine. Mean I = $0{\cdot}023_7$.						
0	$9{\cdot}74_2$	$3{\cdot}65_6$	$3{\cdot}64_9$	−16	$4{\cdot}18_2$	$4{\cdot}22_2$	+40	0—1·1	4	6
10	$9{\cdot}41_7$	$3{\cdot}36_9$	$3{\cdot}43_4$	+71	$4{\cdot}03_1$	$3{\cdot}96_3$	−69	0—1·1	4	9
20	$9{\cdot}13_0$	$3{\cdot}37_6$	$3{\cdot}26_1$	−115	$3{\cdot}71_8$	$3{\cdot}74_5$	+27	0—1·3	4	10
25	—	—	$3{\cdot}18_7$	—	—	$3{\cdot}65_2$				
30	$8{\cdot}87_7$	$3{\cdot}04_2$	$3{\cdot}12_0$	+78	$3{\cdot}62_2$	$3{\cdot}56_7$	−55	0—1·0	4	9
40	$8{\cdot}65_6$	$3{\cdot}02_2$	$3{\cdot}00_6$	−16	$3{\cdot}32_1$	$3{\cdot}42_5$	+104	0—1·2	4	12
50	$8{\cdot}46_3$	$2{\cdot}91_9$	$2{\cdot}91_7$	−2	$3{\cdot}36_1$	$3{\cdot}31_4$	−47	0—1·0	4	8
σ0°, 50°			$0{\cdot}08_3$			$0{\cdot}08_0$				
σ25°			$0{\cdot}05_7$			$0{\cdot}05_5$				

The thermodynamic quantities associated with the formation of the 1 : 1 and 2 : 1 ligand : silver complexes of arginine at 25° and of glycine from 5° to 55° were calculated in the usual way from the constants of equation (3); these are shown in Tables 4 and 5, together with estimates of their errors.[6]

[5] Harned and Robinson, *Trans. Faraday Soc.*, 1940, **36**, 973.
[6] Please, *Biochem. J.*, 1954, **56**, 196.

The temperature coefficient of the constant for the formation of the 1 : 1 glycine : silver complex is remarkable insofar as there is apparently a temperature of maximum stability (11·7°). This is in contrast to the acid dissociation constant of the amino-group of glycine, which diminishes in magnitude with increasing temperature in a manner suggesting that

TABLE 3. *Parameters of equation* (3) *for the formation of silver complexes of arginine and glycine.*

(The charge on the ligand species is given by z.)

	Arginine: $I = 0{\cdot}023_7$; $z = 0$.			Glycine: $I = 0{\cdot}01$; $z = -1$.		
Reaction	*A*	*D*	*C*	*A*	*D*	*C*
$L^z + Ag^{1+} \rightleftharpoons LAg^{z+1}$ ...	3855·2	18·452	0·029208	−7686·3	−57·454	−0·094725
$LAg^{z+1} + L^z \rightleftharpoons L_2Ag^{2z+1}$ ...	4898·35	23·905	0·037321	1506·7	0·763	−0·002879
$LH^{z+1+} \rightleftharpoons L^z + H^{1+}$ ...	−4349·7	−12·654	−0·023694	—	—	—

there is a temperature of minimum stability of the protonated form, albeit far outside the experimental range.[1] This difference is interesting in view of the apparently similar electrostatic changes occurring on the attachment of a silver ion or a proton to the basic

TABLE 4. *Thermodynamic quantities associated with the formation of silver complexes and acid dissociation (amino-group) of arginine at 25°.*

Reaction	I	ΔG (kJ/mole)	ΔH (kJ/mole)	$-\Delta S$ (J/mole-deg.)
$L + Ag^+ \rightleftharpoons LAg^+$	0·0237	−18·19 ± 0·33	−24·1 ± 3·7	20 ± 12
$LAg^+ + L \rightleftharpoons L_2Ag^+$ ...	0·0237	−20·84 ± 0·32	−30·3 ± 3·6	32 ± 12
$L^+ \rightleftharpoons H^+ + L$	0·0237	51·37 ± 0·23	42·9 ± 2·6	28 ± 9
$L^+ \rightleftharpoons H^+ + L$	0	51·320 ± 0·007	44·89 ± 0·08	21·58 ± 0·29

TABLE 5. *Thermodynamic quantities associated with the formation of the silver complexes of glycine.*

Temp.	$-\Delta G$ (kJ/mole)	$-\Delta H$ (kJ/mole) 1 : 1 complex	$-\Delta S$ (J/mole-deg.)	$-\Delta C_p$ (J/mole-deg.)
5°	18·49 ± 0·09	−6·9 ± 2·2	−91 ± 8	1009 ± 86
15	19·22	3·4	−55	1045
25	19·59 ± 0·06	14·0 ± 0·8	−19 ± 3	1081 ± 92
35	19·59	25·0	18	1118
45	19·23	36·3	54	1154
55	18·51 ± 0·09	48·0 ± 2·6	90 ± 8	1190 ± 101
		2 : 1 complex		
25	19·59 ± 0·18	33·7 ± 2·5	47 ± 8	—

glycine amino-group. The value of ΔC_p for the formation of this complex is very large and negative, and the values given in Table 5 are significant despite the magnitude of their errors. Further, the value of ΔG for this process passes through a minimum at 30·1° (see Figure). Any explanation of these phenomena must await results of greater precision.

The values of the thermodynamic quantities associated with the second acid dissociation of arginine at $I = 0{\cdot}0237$, given in Table 4, were obtained from titration-curve data, their errors being similar to those for the values for the formation of the silver complexes. The fact that the former values are consistent, within the limits of error given, with those at $I = 0$ for the same acid dissociation obtained from measurements of high precision in cells without liquid junction [7] may be taken as evidence of the correctness of the estimates of the reliability of these results. The formation of the 1 : 1 arginine : silver complex does not show any of the phenomena described above for the corresponding glycine complex. The values of K_1 diminish continuously with increasing temperature and ΔG becomes

[7] Datta and Grzybowski, in preparation.

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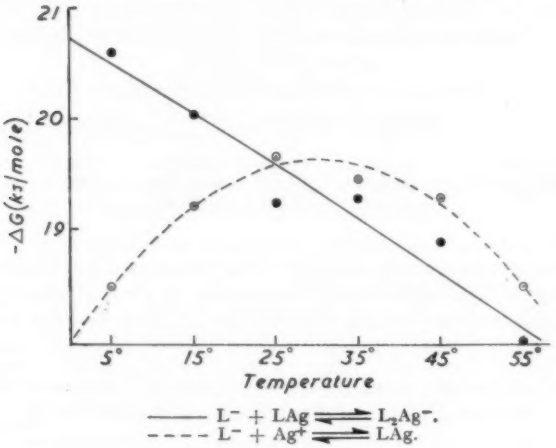
progressively more negative. The sign of ΔS is negative, being opposite to that for the corresponding reaction involving a proton.

The free energy of formation of Ag–*glycine complexes.*



The value of log K_2 for the arginine–silver complex is larger than log K_1 at all the temperatures investigated; with the glycine–silver complexes, on the other hand, log K_2 is larger than log K_1 only up to about 25°, above which temperature log K_1 is the larger.

TABLE 6. *Comparison of the stability constants of silver complexes of ethanolamine and glycine obtained in this work and by other investigators.*

Method *	I [20]	Temp.	pK_a'	log K_1	log K_2	Ref.
			Glycine			
gl.	0	25°	9·78	3·51	3·38	12
Ag	≈0·1	19	—	3·59	3·65	13
gl.	0·5M-KNO_3	20	9·76	3·7	3·3	14
sol.	0	25	9·78	4·28	—	15
gl.	0·01	25	9·66	3·43	3·43	This work
calc.	0·01	20	—	3·47	3·53	,,
			Ethanolamine			
gl.	0·5M-KNO_3	25	9·74	3·13	3·55	16
gl.	0·5M-KNO_3	25	9·60	3·11	3·57	17, 18
gl.	1M-$NaClO_4$	25	9·47	3·12	3·65	19
gl.	0·015	25	9·51	3·29	3·53	This work

* gl. = glass electrode; Ag = silver electrode; sol. = solubility; calc. = calculated.
[13] Monk, *Trans. Faraday Soc.*, 1951, **47**, 292, 297. [13] Dubois, *Compt. rend.*, 1957, **224**, 113. [14] Flood and Lovås, *Tidskr. Kjemi Bergvesen Met.*, 1945, **5**, 83. [15] Keefer and Reiber, *J. Amer. Chem. Soc.*, 1941, **63**, 689. [16] Bruehlman and Verhoek, *ibid.*, 1948, **70**, 1401. [17] Bjerrum, *Chem. Rev.*, 1950, **46**, 381. [18] Bjerrum and Refn, *Suomen Kem.*, 1956, **29**, *B*, 68. [19] Lotz, unpublished results from McIntyre, Doctoral Diss., Pennsylvania State Coll., 1953. Values at 25° have been obtained by interpolation from the data given in " Stability Constants, Part 1," The Chemical Society, 1958, p. 9. [20] The conventions used in indicating the ionic strength are those of *op. cit.*, p. xi.

The differences between the successive stability constants are probably due to an interplay of three factors: (*a*) the statistic effect, which would make log K_2 about 0·6 unit smaller than log K_1, (*b*) the electrostatic effect, which in most cases would tend to weaken the second complex (since the magnitude of this effect will increase with increasing tem-

perature it may account for the crossing over of K_1 and K_2 in the glycine complexes), and (*c*) changes in the electron orbitals involved in complex formation;[8] such changes (*c*) must be of considerable importance in the instances when K_2 is larger than K_1. The present results are compared with those of other workers in Table 6.

Experimental

Glass-electrode pH measurements were made with a Philips pH meter (type GM 4491) for 2-aminoethyl phosphate, 2-aminoethyl sulphate, *NN*-dimethylglycine, ethanolamine, and sarcosine; with a Tinsley vernier potentiometer and an impedance converter for glycine at 5°, 25°, and 45°, and arginine; and with a precision pH meter built in this laboratory by Mr. R. Leberman for glycine at 15°, 35°, and 55° and for 2-amino-2-methylpropane-1 : 3-diol. The cell used for the titrations consisted of a titration vessel and a saturated calomel reference electrode vessel, connected by a glass bridge which was filled with hot potassium nitrate solution which had been saturated at its b. p. On cooling, this bridge solution was practically solid. The ends of the bridge were closed by discs of sintered glass, fused in position.

The titration mixture contained, in most instances, the ligand and silver nitrate only, in the ratios shown in Tables 1 and 2. Arginine, ethanolamine, sarcosine, *NN*-dimethylglycine, and 2-amino-2-methylpropane-1 : 3-diol were only available as the hydrochlorides, and the titration mixtures were prepared by adding an appropriate excess of silver nitrate and filtering off the precipitated silver chloride. Titrations were effected with approx. 0·1M-potassium or sodium hydroxide (carbonate-free). During the titration the solution in the vessel was bubbled with nitrogen to effect mixing and to exclude carbon dioxide.

The cell was standardised in 0·05M-potassium hydrogen phthalate and either 0·01M- or 0·05M-borate.[9,10] All titrations were done in an oil-thermostat, the temperature being maintained within $\pm 0{\cdot}1°$ of the stated value.

All the ligands, except 2-aminoethyl phosphate which was prepared in this laboratory,[11] were purchased. They were purified by recrystallisation, some of them being previously converted into the hydrochlorides. Their purity was checked by titration and, where possible, by gravimetric chloride determinations.

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Department of Biochemistry, University College, London, W.C.1.
Department of Biochemistry and Chemistry,
Guy's Hospital Medical School, London, S.E.1. [*Received, October 15th*, 1958.]

[8] Burkin, *Quart. Rev.*, 1951, **5**, 1.
[9] Bower and Bates, *J. Res. Nat. Bur. Stand.*, 1957, **59**, 261.
[10] British Standards Institution, 1950, 1647.
[11] Clarke, Datta, and Rabin, *Biochem. J.*, 1955, **59**, 209.

223. *Acidity Functions of Some Aqueous Acids.*

By K. N. Bascombe and R. P. Bell.

Measurements have been made of the indicator acidities at 25° of aqueous solutions of sulphuric, phosphorous, methanesulphonic, formic, acetic, monochloroacetic, dichloroacetic, and trichloroacetic acids, several of which were studied over the whole range of compositions. The dissociation constants of several of the indicators were re-determined, and measurements over a range of wavelengths were used to detect effects on the absorption spectra of the indicators due to the medium. Such effects were prominent in the most concentrated solutions of the carboxylic acids, and it is concluded that acidity functions cannot be accurately defined in these solutions. The theoretical treatment previously developed for solutions of strong acids is used to derive an approximate value of 4 for the dissociation constant of methanesulphonic acid.

The Hammett acidity function has been widely used in assessing the mechanistic significance of kinetic measurements in concentrated acid solutions, and recent reviews [1,2] have dealt thoroughly with this subject. There is also a close connection between indicator acidities and the general problem of interpreting the equilibrium properties of concentrated electrolyte solutions.[3,4] Nevertheless, a large proportion of the available experimental data is derived from Hammett's pioneer work, which employed a visual colorimeter without temperature control. The present paper reports measurements at 25°, in which a spectrophotometer was used, and special attention was paid to limitations upon the accuracy with which the acidity function can be defined or measured. In particular, measurements were carried out over a range of wavelengths, so as to detect any effect of changes in the medium on the absorption spectra of the species concerned. Many of the measurements relate to solutions of weak acids which have not previously been fully investigated.

Experimental

Of the acids used, perchloric, hydrochloric, sulphuric, acetic, formic, monochloroacetic trichloroacetic, and iodic were " AnalaR " products. Phosphorous, dichloroacetic, and toluene-*p*-sulphonic acids were of " Laboratory Reagent " grade, the last being recrystallised from alcohol. Methanesulphonic acid was manufactured by Boots Pure Drug Co., Ltd., and its purity checked by titration.

The following indicators were B.D.H. Laboratory Reagents, recrystallised from alcohol, and having m. p. within 2° of the accepted value: *p*-aminoazobenzene, *m*-nitroaniline, phenylazodiphenylamine, *p*-nitroaniline, *o*-nitroaniline, *p*-nitrodiphenylamine, 2 : 4-dinitroaniline, benzylideneacetophenone, and *NN*-dimethyl-*p*-nitroaniline. 4-Chloro-2-nitroaniline was a laboratory specimen recrystallised from alcohol. 4-Methyl-2 : 6-dinitroaniline was prepared as described by Brady, Day, and Rolt [5] (m. p. 165° from alcohol). 6-Bromo-2 : 4-dinitroaniline was prepared by brominating 2 : 4-dinitroaniline in glacial acetic acid at 100° (cf. Elion [6]). The product separated on cooling and was filtered off, washed with water, dried, and twice recrystallised from alcohol (m. p. 151°). *NN*-Dimethyl-2 : 4-dinitroaniline was prepared by adding solid *NN*-dimethyl-*p*-nitroaniline to excess of 1 : 1 aqueous nitric acid. The amine dissolved, but after a few minutes yellow crystals of the nitrate of the required product began to separate. After half an hour the mixture was neutralised with an excess of aqueous sodium hydroxide and the solid product filtered off, washed with water, dried, and recrystallised from alcohol (m. p. 86°).

The acid solutions were standardised by volume either against borax, or (through sodium hydroxide solution) against constant-boiling hydrochloric acid. The weight concentrations

[1] Paul and Long, *Chem. Rev.*, 1957, **57**, 1.
[2] Long and Paul, *Chem. Rev.*, 1957, **57**, 935.
[3] Bascombe and Bell, *Discuss. Faraday Soc.*, 1957, **24**, 158.
[4] Wyatt, *Discuss. Faraday Soc.*, 1957, **24**, 162.
[5] Brady, Day, and Rolt, *J.*, 1922, 527.
[6] Elion, *Rec. Trav. chim.*, 1923, **42**, 171.

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given in the Tables were calculated from published densities, supplemented by our measurements on solutions of phosphorous and methanesulphonic acids. Stock indicator solutions were made up by weight in water or in the acid solution being investigated and the solutions for measurement were made by adding a known weight of indicator solution to a much larger volume of acid solution, giving indicator concentrations of about 10^{-5}M. The same indicator stock solution was used for measuring the absorption of the acidic and the basic form of the indicator and of the solution being investigated, so that it was not necessary to know its concentration accurately.

Optical densities were measured with a Unicam S.P. 500 spectrophotometer with a cell compartment regulated at 25° ± 0·02°. The latter consisted of a metal block resembling that described by Evans, Herington, and Kynaston:[7] the temperature was controlled by a platinum resistance thermometer embedded in the block, which formed one arm of a Wheatstone bridge and actuated a relay. The optical-density scale was tested by making measurements with solutions of potassium chromate which have been shown[8] to obey Beer's law with high accuracy. The apparent extinction coefficient at a given wavelength varied with concentration, decreasing by 2% for each unit increase in optical density. This shows that the scale of the instrument is slightly in error, and the true optical densities (D) were calculated from those read from the scale (D^*) by the relation $D = 50D^*/(50 - D^*)$. Similar difficulties in the accurate use of the Unicam S.P. 500 instrument have been reported by Davies and Prue.[9]

All measurements employed stoppered 10 mm. silica cells which were optically matched. Water was used in the comparison cell, and measurements were made over a range of 1000—1500 Å at intervals of 100 or 200 Å. In any set of measurements the observed optical densities (after application of the correction described above) were converted to a standard indicator concentration, usually that used in measuring the spectrum of the basic form of the indicator: these converted optical densities are represented by D'.

The acidity function H_0, as measured by an uncharged basic indicator B, is defined by

$$H_0 = pK + \log [B]/[BH^+] = pK + \log (D' - D'_{BH^+})/(D'_B - D') \quad . \quad . \quad (1)$$

where pK refers to BH^+, and D'_{BH^+} and D'_B are the converted optical densities for solutions in which the indicator is present entirely in the acidic and in the basic form respectively. D'_{BH^+} was usually measured in sulphuric acid of about 50% concentration. It was much smaller than D'_B for all the indicators used, with the exception of benzylideneacetophenone, which was used only for a few measurements with methanesulphonic acid: it was therefore not necessary to know D'_{BH^+} accurately. Indicators with p$K > -1$ are appreciably protonated even in dilute acid solution, and for these the value of D'_B was measured in 0·1M-aqueous sodium hydroxide. Since these indicators were not used in very concentrated acid solutions it is reasonable to use this value throughout in calculating H_0 from eqn. (1). The validity of this assumption can be tested to some extent by making measurements at different wavelengths, since it is unlikely that a change of medium would change the value of D'_B at a given wavelength without also changing the shape of the absorption curve. This test was carried out in most of the measurements, and examples are given under the individual acids. The most weakly basic indicators (pK −3 to −7) were used in very concentrated acid solutions, sometimes up to 100% acid, and it is certainly not appropriate to use the value of D'_B measured in water or dilute alkali. In most instances D'_B was measured in a solution of the acid being studied just below the concentration range in which protonation begins to become appreciable: this procedure was used by Hammett and Deyrup.[10] However, other procedures are possible and their use does not lead to identical results in concentrated solutions, as illustrated by our measurements with *p*-nitrodiphenylamine in sulphuric acid. The same uncertainty is revealed by the apparent variation of indicator ratio when the same solution is investigated at different wavelengths.

The indicators used, together with the values assumed for pK_a, are listed in Table 1. The pK values for the first three indicators were obtained from measurements in dilute solutions of hydrochloric, perchloric, and toluene-*p*-sulphonic acid, which were assumed to be completely

[7] Evans, Herington, and Kynaston, *Trans. Faraday Soc.*, 1953, **49**, 1284.
[8] Kortüm, *Z. phys. Chem.*, 1936, *B*, **33**, 243.
[9] Davies and Prue, *Trans. Faraday Soc.*, 1955, **51**, 1045.
[10] Hammett and Deyrup, *J. Amer. Chem. Soc.*, 1932, **54**, 4239.

dissociated. As would be expected in very dilute solution, the observed values of log {[BH^+]/[B][H^+]} showed no trend with acid concentration, and the values given for pK are averages for all measurements. As an example the results for *p*-aminoazobenzene are given in Table 2. The limits of error given for the indicator ratio I and the value of log {[BH^+]/[B][H^+]} calculated from it are based upon the precision and reproducibility of the instrumental readings.

TABLE 1. pK *values of indicators.*

	Indicator	pK (i)	Method	pK (ii)
I.	*p*-Aminoazobenzene	2·82	(a)	2·76
II.	*m*-Nitroaniline	2·50	(a)	2·50
III.	*p*-Nitroaniline	1·02	(a)	0·99
IV.	*o*-Nitroaniline	−0·29	(c)	−0·29
V.	*NN*-Dimethyl-2 : 4-dinitroaniline	−1·00	(c)	—
VI.	4-Chloro-2-nitroaniline	−1·02	(c)	−1·03
VII.	*p*-Nitrodiphenylamine	−2·4 to −2·9	(c)	−2·50
VIII.	4 : 6-Dichloro-2-nitroaniline	−3·61	(b)	−3·32
IX.	4-Methyl-2 : 6-dinitroaniline	−3·96	(b)	−4·44
X.	6-Bromo-2 : 4-dinitroaniline	−6·64	(b)	−6·71

(i) Present paper.
(ii) " Best value " given by Paul and Long.[1]
(a) Measured directly in dilute solutions of strong acids. (b) From overlap in solutions of methanesulphonic acid. (c) From overlap in solutions of sulphuric acid.

Table 2 shows that the observed indicator ratio is independent of the wavelength, and the same is true for *m*-nitroaniline and *p*-nitroaniline. The values obtained for the pK of these indicators agree fairly well with the " best values " of Paul and Long.[1] The values obtained for the remaining seven indicators are discussed in connection with the measurements on solutions of sulphuric and methanesulphonic acids.

Results.—In the Tables the indicators are numbered as in Table 1. Unless otherwise stated, measurements were made at the wavelengths of maximum absorption of the basic form, which were as follows: I 3800 Å, II 3600 Å, III 3800 Å, IV 4100 Å, V 3900 Å, VI 4200 Å, VII 4100 Å, VIII 4200 Å, IX 4500 Å, X 3550 Å. The acid concentration (concn.) is in moles/l. Details follow for the individual acids.

TABLE 2. *Measurement of* pK *for* p*-aminoazobenzene.*

[HCl]	I	log {[BH^+]/[B][H^+]}	[*p*-Me·C_6H_4·SO_3H]	I	log {[BH^+]/[B][H^+]}
0·00358	2·25 ± 0·12	2·80 ± 0·03	0·00171	1·17 ± 0·03	2·83 ± 0·01
0·00366	2·65 ± 0·09	2·86 ± 0·02	0·00435	2·75 ± 0·09	2·80 ± 0·02
	2·60 ± 0·09 *	2·84 ± 0·02		2·79 ± 0·08 *	2·82 ± 0·02
	2·73 ± 0·09 †	2·89 ± 0·02		2·68 ± 0·08 †	2·77 ± 0·02
0·00540	3·66 ± 0·12	2·83 ± 0·02	0·00870	5·73 ± 0·26	2·82 ± 0·02
0·00658	3·87 ± 0·15	2·77 ± 0·03			
0·00715	4·96 ± 0·17	2·84 ± 0·02			
0·00880	5·94 ± 0·18	2·83 ± 0·02			
[$HClO_4$]					
0·00087	0·53 ± 0·02	2·78 ± 0·02			
0·00266	1·72 ± 0·04	2·81 ± 0·01			
0·0455	2·94 ± 0·06	2·81 ± 0·01			
	2·98 ± 0·06 *	2·83 ± 0·01			
	2·95 ± 0·06 †	2·81 ± 0·01			
0·00957	7·10 ± 0·27	2·87 ± 0·02			

I = [BH^+]/[B].
Measurements at 3800 Å unless otherwise stated.
* Measurements at 3600 Å.
† Measurements at 4000 Å.

Sulphuric acid. This was studied in order to check the pK values for some of the indicators, and also to provide more accurate data for the intermediate range of concentrations. Most of the results are given in Table 3; they are independent of the wavelength within experimental error (2—5% in I, or 0·01 to 0·02 in H_0, depending upon the value of I and the part of the instrumental scale being used). The values of H_0 derived from indicators I, II, and III are in good mutual agreement, by use of the pK values in Table 1, and up to a concentration of c = 0·01 they agree within 0·02 unit with $H_0 = -\log [H^+]$, where [H^+] is calculated from $f_2\,[H^+]([H^+] - c)/(2c - [H^+]) = 0{\cdot}0103$, where f_2 is given in terms of the ionic strength μ by $-\log f_2 = 2\mu^{\frac{1}{2}}/(1 + \mu^{\frac{1}{2}})$. This calculation assumes that $f_{H^+} = f_{HSO_4^-}$, and the ionic strength is

obtained by successive approximations, while $K = 0{\cdot}0103$ is the value given by Davies, Jones, and Monk [11] for the second dissociation constant of sulphuric acid.

The pK values for indicators IV, V, and VI have been chosen to give concordant values of H_0 in the region of overlap, as shown in Table 3. pK(IV) and pK(VI) are in good agreement with the best values of Paul and Long [1] (cf. Table 1). Indicator V has not previously been investigated, and is of interest in being a tertiary amine: nevertheless, it gives results closely parallel with those of the primary amine VI of similar pK. The indicator *NN*-dimethyl-2 : 4 : 6-

TABLE 3. *Sulphuric acid.*

Key to wavelengths (λ): *m* maximum absorption, *a* 3400 Å, *b* 3600 Å, *c* 3700 Å, *d* 3800 Å, *e* 3900 Å, *f* 4000 Å, *g* 4400 Å, *h* 4600 Å.

Concn.	Wt. %	Indr.	λ	I	H_0	Concn.	Wt. %	Indr.	λ	I	H_0
0·00050	0·0049	I	*m*	0·62	3·03			III	*b*	28·6	−0·44
0·00058	0·0057	I	*m*	0·76	2·94			III	*c*	28·2	−0·43
		I	*b*	0·80	2·92	1·20	10·9	III	*m*	28·7	−0·44
0·00059	0·0058	I	*m*	0·76	2·94			III	*e*	29·0	−0·44
		I	*f*	0·78	2·93			III	*f*	29·0	−0·44
		I	*b*	1·02	2·81			IV	*d*	1·45	−0·44
0·00067	0·0066	I	*m*	0·98	2·83	1·22	11·1	IV	*m*	1·49	−0·46
		I	*f*	1·02	2·81			IV	*g*	1·47	−0·45
0·00098	0·0096	I	*m*	1·13	2·77	1·49	13·4	IV	*m*	2·13	−0·62
0·00118	0·0116	I	*m*	1·43	2·67	1·54	13·8	VI	*m*	0·415	−0·64
0·00134	0·0131	I	*m*	2·04	2·51	1·56	14·1	IV	*m*	2·43	−0·68
0·00239	0·0234	I	*m*	2·99	2·35	1·57	14·2	III	*m*	48·3	−0·66
0·00253	0·0248	I	*m*	3·09	2·33	1·66	14·75	III	*m*	53·3	−0·71
0·00409	0·0401	I	*m*	4·84	2·14	1·85	16·3	IV	*m*	3·51	−0·83
0·00434	0·0425	I	*m*	5·07	2·12	1·86	16·4	VI	*m*	0·65	−0·83
0·00480	0·0470	I	*m*	5·48	2·08	1·91	16·8	VI	*m*	0·72	−0·88
0·00603	0·0590	I	*m*	6·8	1·99	1·94	17·1	IV	*m*	3·74	−0·86
0·00615	0·0602	II	*m*	3·34	1·98			III	*b*	81	−0·89
0·00750	0·0734	I	*m*	8·3	1·90	2·04	17·8	III	*m*	83	−0·90
0·00908	0·0890	I	*m*	9·8	1·83			III	*f*	82	−0·90
		II	*a*	7·6	1·62	2·20	19·1	V	*m*	0·84	−0·93
0·0139	0·136	II	*m*	7·1	1·65			VI	*f*	1·57	−1·22
		II	*d*	7·0	1·66	2·61	22·2	VI	*m*	1·55	−1·21
		II	*a*	12·4	1·41			VI	*g*	1·53	−1·20
0·0254	0·248	II	*m*	12·1	1·42	2·68	22·6	IV	*m*	9·1	−1·25
		II	*d*	11·3	1·45	2·95	24·6	V	*m*	2·38	−1·38
0·0333	0·325	II	*m*	15·6	1·32	2·95	24·6	VI	*m*	2·30	−1·38
0·0410	0·400	III	*m*	0·63	1·22			IV	*d*	13·2	−1·40
0·0625	0·612	III	*m*	0·91	1·06	3·02	25·1	IV	*m*	13·6	−1·42
0·235	2·26	III	*m*	3·44	0·48			IV	*g*	13·5	−1·42
0·278	2·67	III	*m*	4·11	0·41	3·55	28·7	V	*m*	5·21	−1·72
0·280	2·69	III	*m*	4·14	0·40	3·55	28·7	VI	*m*	4·38	−1·66
0·355	3·39	III	*m*	5·47	0·28	4·29	33·6	V	*m*	10·8	−2·03
0·540	5·10	III	*m*	8·5	0·09	4·33	33·8	IV	*m*	75	−2·16
0·90	8·3	III	m	17·3	−0·22	4·54	35·2	V	*m*	14·1	−2·15
0·90	8·3	IV	*m*	0·89	−0·24			VI	*f*	15·9	−2·22
0·98	9·1	III	*m*	19·5	−0·27	4·61	35·6	VI	*m*	15·9	−2·22
1·18	10·75	III	*m*	27·7	−0·42			VI	*g*	15·5	−2·21
						4·84	37·1	V	*m*	23·7	−2·37
						5·08	38·6	VI	*m*	26·7	−2·45

trinitroaniline gives ionisation curves in 65—75% aqueous sulphuric acid and in acetic acid solutions of sulphuric acid which deviate considerably from those given by primary amines,[10,12] but individual deviations are more prominent in these highly acid solutions.

Attempts were made to study sulphuric acid solutions more concentrated than 5M by using indicator VII (*p*-nitrodiphenylamine). Since this will not be appreciably protonated at concentrations less than about 2M, it is possible to investigate the effect of acid concentration upon D'_B, the absorption of the basic form. Table 4 shows the results for three wavelengths in the neighbourhood of the maximum (4100 Å). It is clear that there is a considerable medium effect, which varies with wavelength. Three different assumptions have been made in calculating the indicator ratios in the range 4M—7M-sulphuric acid: (i) D'_B has the same value as in

[11] Davies, Jones, and Monk, *Trans. Faraday Soc.*, 1952, **48**, 921.
[12] Hall and Spengemann, *J. Amer. Chem. Soc.*, 1940, **62**, 2487.

neutral aqueous solution. (ii) D'_B has the same value as in 1·8M-sulphuric acid (*i.e.*, just below the protonation range). (iii) D'_B is calculated from Table 4 by linear extrapolation to the relevant acid concentration. Table 5 shows the results of these three assumptions. The values of I differ considerably according to the assumption made about D'_B: with assumptions (i) and (ii) there is also a considerable variation with wavelength, but with assumption (iii)

TABLE 4. *Medium effect on the absorption of* p-*nitrodiphenylamine.*

	$[H_2SO_4]$	0·575	0·98	1·38	1·83
D'_B	3800 Å	2·82	2·87	2·85	2·89
	4100 Å	3·80	3·90	3·94	4·05
	4400 Å	2·50	2·61	2·72	2·76

this variation is no greater than the uncertainty in the extrapolation for obtaining D'_B. However, this may be coincidental, since the values of I on assumption (iii) are not consistent with the results of Table 3 obtained with indicators IV, V, and VI. The choice of $pK = -2·4$ for *p*-nitrodiphenylamine gives coincident values of H_0 at 4·4M, but the plots of H_0 against Concn. diverge sharply at higher concentrations. On the other hand, either assumption (i) with $pK = -2·93$ or assumption (ii) with $pK = -2·60$ leads to values of H_0 which are consistent with Table 3. The values of H_0 from measurements at 4100 Å are given in Table 6: as can be seen from Table 5, somewhat different values would be obtained by using other wavelengths.

TABLE 5. *Apparent indicator ratios for* p-*nitrodiphenylamine in sulphuric acid.*

		I					*I*		
Concn.	λ (Å)	(i)	(ii)	(iii)	Concn.	λ (Å)	(i)	(ii)	(iii)
4·38	3800	0·199	0·384	0·465	6·36	3800	1·80	2·23	2·54
	4100	0·156	0·323	0·495		4100	1·64	2·03	2·72
	4400	0·130	1·290	1·457		4400	1·33	1·54	2·55
4·87	3800	0·328	0·532	0·665	7·04	3800	4·39	5·21	6·3
	4100	0·268	0·457	0·684		4100	4·31	5·09	6·7
	4400	0·226	0·305	0·644		4400	3·80	4·19	6·8
5·68	3800	0·673	1·08	1·25					
	4100	0·644	0·89	1·26					
	4400	1·516	0·63	1·28					

Tables 4—6 illustrate the difficulties which can arise in more concentrated solutions and the consequent uncertainties in H_0. These uncertainties arise partly from effects of the medium upon absorption spectra, and partly from a more fundamental breakdown in the concept of acidity functions, in that H_0 may no longer be independent of the indicator used for its measurement. It is probable that these medium effects are particularly large for *p*-nitrodiphenylamine, since most of the other indicators showed a much smaller dependence of apparent indicator ratio upon wavelength even when no allowance was made for the variation of D'_B with concentration.

TABLE 6. H_0 *from* p-*nitrodiphenylamine in sulphuric acid.*

(All measurements at 4100 Å, maximum.)
pK for indicator: (i) −2·93, (ii) −2·60, (iii) −2·40.

Concn.	Wt. %	Assumption	D'_B	*I*	H_0	Concn.	Wt. %	Assumption	D'_B	*I*	H_0
4·38	34·2	i	3·53	0·156	−2·11	6·36	45·9	i	3·53	1·64	−3·14
		ii	4·05	0·323	−2·11			ii	4·05	2·03	−2·91
		iii	4·57	0·495	−2·10			iii	4·97	2·72	−2·84
4·87	37·2	i	3·53	0·268	−2·36	7·04	49·6	i	3·53	4·31	−3·57
		ii	4·05	0·457	−2·26			ii	4·05	5·09	−3·31
		iii	4·67	0·68	−2·24			iii	5·10	6·70	−3·33
5·68	42·2	i	3·53	0·64	−2·74						
		ii	4·05	0·89	−2·55						
		iii	4·83	1·26	−2·50						

The values of H_0 in Tables 3 and 6 are in general agreement with Hammett and Deyrup's measurements [10] as recalculated by Paul and Long,[1] but show much less scatter.

Methanesulphonic acid. This acid was studied over the whole concentration range 0—100%,

partly in order to provide pK-values for indicators VIII, IX, and X, and partly because of the interest of an acid slightly weaker than the common mineral acids. Of the eight indicators used two were unsatisfactory. *p*-Nitrodiphenylamine gave inconsistent results, and appeared to react slowly with the acid. With benzylideneacetophenone the basic form has no absorption in the range usually examined, while the protonated form has a peak at 4300 Å in concentrated sulphuric acid. This appears at 4100 Å in 100% methanesulphonic acid; on addition of water the extinction coefficient increases by 30% in 95% acid, and then falls in the range 80—90%, simultaneously shifting to 3900 Å. This behaviour suggests either that several species are present or that the absorption spectra are subject to large medium effects: in either event the indicator is unsuitable for measuring acidities. The results for the remaining indicators are given in Table 7.

TABLE 7. *Methanesulphonic acid.*

Key to wavelengths: *m* maximum absorption, *a* 3300 Å, *b* 3400 Å, *c* 3800 Å, *d* 4200 Å, *e* 4400 Å, *f* 4600 Å, *g* 4800 Å.

Concn.	Wt. %	Indr.	λ	I	H_0	Concn.	Wt. %	Indr.	λ	I	H_0
0·302	3·0	III	*m*	2·72	0·43			VIII	*c*	0·165	−2·82
		III	*b*	11·0	−0·02	8·32	61·5	VIII	*m*	0·151	−2·79
0·749	6·8	III	*m*	11·3	−0·03			VIII	*f*	0·170	−2·84
		III	*c*	11·5	−0·04	9·38	67·4	VIII	*m*	0·538	−3·34
1·557	13·9	III	*m*	24·7	−0·37	10·46	73·3	VIII	*m*	1·99	−3·91
		IV	*c*	1·78	−0·54			IX	*d*	1·23	−4·05
1·925	17·0	IV	*m*	1·81	−0·55	10·78	74·9	IX	*m*	1·21	−4·04
		IV	*e*	1·77	−0·54			IX	*g*	1·20	−4·04
2·51	21·9	IV	*m*	2·28	−0·65	10·85	75·3	VIII	*m*	2·91	−4·07
2·98	25·5	VI	*m*	0·59	−0·79	11·85	80·6	VIII	*m*	9·6	−4·59
3·30	28·0	VI	*m*	0·72	−0·88	12·12	82·1	IX	*m*	7·6	−4·84
		VI	*c*	2·18	−1·36	12·74	85·2	IX	*m*	26·7	−5·39
4·82	39·5	VI	*m*	2·27	−1·38	13·45	88·9	X	*m*	0·309	−6·12
		VI	*f*	2·18	−1·36	13·95	91·4	X	*m*	0·94	−6·61
6·16	48·3	VI	*m*	7·4	−1·89			X	*a*	6·4	−7·44
6·44	50·2	IV	*m*	56·9	−2·05	14·77	95·7	X	*m*	6·1	−7·42
7·15	54·5	VI	*m*	19·1	−2·30			X	*c*	6·3	−7·43
						15·07	100·0	X	*m*	16·7	−7·86

There is no detectable variation of apparent indicator ratio with wavelength for any of the indicators studied, even close to 100% acid. The pK values taken for indicators III, IV, and VI are those previously obtained, while those for VIII, IX, and X are chosen so as to give good overlap or alignment in the present set of measurements (cf. Table 1). The values for VIII and IX differ somewhat from Paul and Long's best values, but the latter are based mainly on Hammett's early measurements with sulphuric acid and the differences probably reflect the spread of his experimental data in this region of concentration.

Trichloroacetic acid. An " AnalaR " specimen showed a small absorption in the range 3500—4500 Å, which was increased by vacuum distillation. The unpurified acid was therefor used, and a small correction applied. The results are given in Table 8.

TABLE 8. *Trichloroacetic acid.*

Measurements at peak wavelength, except those marked *a* (3400 Å), *b* (3800 Å), *c* (4200 Å), *d* (4400 Å).

Concn.	Wt. %	Indr.	I	H_0	Concn.	Wt. %	Indr.	I	H_0
0·221	4·0	IV	0·111	0·67	3·89	49·5	III	9·5	+0·04
0·574	9·1	IV	0·306	0·22			III	11·4 (*a*)	−0·03
		IV	0·435 (*b*)	0·07	4·99	59·9	III	10·8	−0·01
0·786	12·5	IV	0·406	1·10			III	10·9 (*c*)	−0·01
		IV	0·429 (*d*)	0·08			IV	1·12 (*b*)	−0·34
1·07	16·6	IV	0·509	0·00	6·68	74·0	IV	1·07	−0·32
1·72	25·5	III	10·7	−0·01			IV	1·12 (*d*)	−0·34
		III	10·8 (*a*)	0·00	7·26	78·6	III	34·3	−0·53
2·70	37·0	III	10·4	+0·01					
		III	10·0 (*c*)	+0·02					

The results are satisfactorily independent of wavelength, and the two indicators give concordant values. If allowance is made for the different pK values taken for *p*-nitroaniline, our

results agree fairly well with those of Randles and Tedder,[13] who allowed for the absorption of the acid solution, but they are much lower than the three measurements reported by Hammett and Paul,[14] who made no such allowance.

Dichloroacetic acid. Measurements were made over the whole range of composition 0—100% with three indicators, but only the measurements with *p*-nitroaniline are recorded in Table 9. *o*-Nitroaniline and 4-chloro-2-nitroaniline were used in the range 80—100% acid, but the apparent indicator ratios varied greatly with wavelength in the neighbourhood of maximum absorption, and no reliance can be placed on the results.

The values in Table 9 agree fairly well with the less accurate measurements of Bell and Brown [15] when allowance is made for the different pK values assumed for the indicator.

Monochloroacetic acid. Measurements were extended up to the saturated solution (82%) and are given in Table 10.

TABLE 9. *Dichloroacetic acid.*

Indicator *p*-nitroaniline. Measurements at peak wavelength, except those marked *a* (3400 Å) or *b* (4200 Å)

Concn.	Wt. %	I	H_0	Concn.	Wt. %	I	H_0
0·281	3·1	1·18	0·95	5·49	55·5	2·51	0·62
0·558	6·8	1·76	0·77	6·46	63·0	3·03	0·54
1·098	13·1	2·32	0·65	7·28	68·4	3·65	0·46
2·35	26·9	2·34	0·65			5·37 (*a*)	0·29
		2·34 (*a*)	0·66	8·35	76·4	5·33	0·29
2·93	33·0	2·37	0·65			5·68 (*b*)	0·26
		2·15 (*b*)	0·61			11·5 (*a*)	−0·05
3·44	37·8	2·28	0·66	9·76	85·5	15·7	−0·19
		2·43 (*a*)	0·64			15·9 (*b*)	−0·19
5·07	52·0	2·36	0·65				
		2·29 (*b*)	0·66				

TABLE 10. *Monochloroacetic acid.*

All measurements with *p*-nitroaniline, except those marked *, which are with *p*-aminoazobenzene. Measurements at peak wavelength, except those marked *a* (3400 Å) or *b* (4200 Å).

Concn.	Wt. %	I	H_0	Concn.	Wt. %	I	H_0
		0·217 (*a*)	1·68			0·420 (*a*)	1·39
0·363	3·38	0·234	1·65	4·90	40·0	0·396	1·42
		0·226 (*b*)	1·66			0·432 (*b*)	1·38
0·684	6·30	0·276	1·58			0·499 (*a*)	1·32
0·728	6·70	0·277	1·58	6·67	52·2	0·535	1·29
0·748	6·89	17·7 *	1·57			0·625 (*b*)	1·23
1·357	12·24	0·322	1·51	7·40	56·7	0·624	1·23
1·462	13·12	0·352	1·47			0·780 (*a*)	1·13
2·10	18·4	0·361	1·46	8·06	60·9	0·762	1·14
2·13	18·8	0·360	1·46			1·18 (*b*)	0·94
2·17	19·1	0·366	1·46			1·45 (*a*)	0·86
2·19	19·3	0·363	1·46	9·36	68·8	1·58	0·82
2·40	21·0	22·0 *	1·48			2·11 (*b*)	0·68
2·75	23·8	0·354	1·47			2·03 (*a*)	0·72
2·87	24·7	0·364	1·46	10·86	77·4	2·07	0·70
3·29	28·0	0·362	1·46			2·65 (*b*)	0·60
		0·346 (*a*)	1·48			1·77 (*a*)	0·76
3·33	28·3	0·358	1·47	11·21	79·3	2·06	0·70
		0·347 (*b*)	1·48			2·86 (*b*)	0·57
3·43	29·1	0·362	1·46			0·99 (*a*)	1·02
3·56	30·1	0·363	1·46	11·65	81·6	1·11	0·98
4·59	37·8	22·5 *	1·47			1·40 (*b*)	0·88

The results of measurements with indicators I and III are in good agreement, but for solutions more concentrated than about 50% there is a considerable dependence on wavelength, and in this region the H_0 scale is certainly not defined to better than about ±0·1.

Formic acid. With this acid the observed optical densities changed with time, possibly

[13] Randles and Tedder, *J.*, 1955, 1218.
[14] Hammett and Paul, *J. Amer. Chem. Soc.*, 1934, **56**, 827.
[15] Bell and Brown, *J.*, 1954, 774.

because of slow reaction between the acid and the amines (cf. Davis [16]). It was possible to extrapolate back to zero time with fair accuracy, but the results were still unsatisfactory. Measurements with indicator II suggested only small variations of H_0 in the range 1·6—2·0 for 7—80% formic acid solutions. By contrast, the use of indicators III and IV produced H_0 values which decrease continuously by more than 3 units over the same range of concentrations: however, with the pK values of Table 1 there is a discrepancy of about 0·25 unit between the values of H_0 derived from these two indicators. It is therefore not possible to define an acidity scale on the basis of these measurements. Because of the variation with time, measurements were carried out at the peak wavelength only.

Acetic acid. Measurements were carried out over the whole range of compositions: there was no change with time during the time necessary for measurement, but it was not found possible to define an acidity scale. Indicator II at its peak wavelength showed very small changes in indicator ratio in the range 5—85% acetic acid, corresponding to H_0 values in the range 2·25—2·45, but the use of different wavelengths introduced discrepancies of up to 0·3 in H_0. In confirmation of this, both nitrobenzene and 2 : 4-dinitroaniline (which are not appreciably protonated in the solutions used) showed considerable changes in absorption spectra when the acetic acid concentration was varied from 5% to 85%. Measurements with indicator I suggested a decrease of H_0 from 2·3 to 1·9 in the range 7—60% acetic acid, but there is no reason to believe that this result is reliable. The most that can be said is that there are no very large changes in indicator acidity in the range 5—85%.

Phosphorous acid. This was investigated up to the limit of solubility (about 50%) with indicators III, IV, and VI, and the results are given in Table 11. There is satisfactory agreement between the different indicators, but the effect of varying the wavelength shows that there are increasing uncertainties in the acidity scale above about 20% acid.

TABLE 11. *Phosphorous acid.*

Key to wavelengths: *m* maximum absorption, *a* 3400 Å, *b* 3800 Å, *c* 4200 Å, *d* 4400 Å, *e* 4600 Å.

Concn.	Wt. %	Indr.	λ	I	H_0	Concn.	Wt. %	Indr.	λ	I	H_0
0·096	0·436	III	*m*	0·57	1·26	6·04	22·7	IV	*m*	1·22	−0·38
0·235	1·06	III	*m*	1·16	0·96			IV	*b*	1·36	−0·43
		III	*a*	2·31	0·65	7·46	26·9	IV	*m*	1·76	−0·54
0·596	2·66	III	*m*	2·23	0·67			IV	*d*	1·55	−0·48
		III	*c*	2·17	0·68	8·32	29·6	VI	*m*	0·408	−0·63
		IV	*b*	0·188	0·43			VI	*b*	0·181	−0·28
0·99	4·36	IV	*m*	0·208	0·39	9·38	32·6	VI	*m*	0·449	−0·67
		IV	*d*	0·181	0·45			VI	*e*	0·373	−0·59
		III	*a*	4·77	0·34	10·24	35·8	IV	*m*	3·21	−0·80
1·18	5·15	III	*m*	5·12	0·31	10·86	37·2	VI	*m*	0·78	−0·91
		III	*c*	4·46	0·36	12·05	40·8	IV	*m*	4·75	−0·97
		IV	*b*	0·307	0·22	12·50	42·2	VI	*m*	1·08	−1·05
2·01	8·55	IV	*m*	0·322	0·20			VI	*b*	0·68	−0·86
		IV	*d*	0·288	0·25	13·8	46·1	VI	*m*	2·07	−1·34
		IV	*b*	0·585	−0·05			VI	*e*	1·71	−1·25
4·01	15·6	IV	*m*	0·619	−0·08						
		IV	*d*	0·627	−0·09						

Iodic acid. No satisfactory measurements were obtained with this acid. The "AnalaR" material gave a cloudy solution in water. Clear solutions 0·2—1·6M were obtained after recrystallisation, but their acidity towards *p*-nitroaniline decreased slowly on keeping, without reaching any steady value. This phenomenon may be due to a slow polymerisation or depolymerisation of iodic acid species in solution. The existence of polymerised species has been suggested several times, but the constitution of these solutions is obscure.[17]

DISCUSSION

The above measurements provide revised pK values for a number of indicators (including one new one, *NN*-dimethyl-2 : 4-dinitroaniline) and for the acidity functions of solutions of sulphuric, trichloroacetic, and dichloroacetic acids. Solutions of methanesulphonic, monochloroacetic, and phosphorous acid were investigated for the first time, and measurements were also made with solutions of acetic, formic, and iodic acids, though it

[16] Davis, *Z. phys. Chem.*, 1912, **78**, 353.
[17] Morgan, *Quart. Rev.*, 1954, **8**, 123.

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was not possible to define any reliable acidity functions for the last three. Our measurements show that under favourable conditions it is possible to define H_0 with an accuracy of about 0·02 unit, and it is noteworthy that this is the case for methanesulphonic acid over the whole range of compositions, the pure acid having $H_0 = -7{\cdot}86$. Trichloroacetic acid also gives a satisfactory acidity scale up to the solubility limit of 79% acid, and dichloroacetic acid up to about 80%. However, measurements at different wavelengths show that the spectra of indicators often show considerable changes in concentrated solutions of weak acids, and this was specially marked for acetic, formic, and monochloroacetic acids. Under these conditions the acidity function cannot be accurately defined, and it is dangerous to draw conclusions from measurements at a single wavelength. The indicator *p*-nitrodiphenylamine shows large medium effects even with sulphuric acid solutions, and it is unfortunate that no other indicator has been investigated between pK −1 and pK −3.

Solutions of phosphorous acid show a steady increase of acidity over the concentration range investigated, thus resembling all other inorganic acids which have been studied. In the intermediate range of concentrations the values of H_0 resemble those for orthophosphoric acid and potassium hydrogen sulphate, which have similar dissociation constants.* The three chloroacetic acids (and also trifluoroacetic acid [13]) show quite a different type of behaviour, in that the acidity is almost independent of concentration over the range 1—5M, and is much less than for an inorganic acid of similar dissociation constant. The cause of this behaviour is obscure, but it is possible that, as suggested by Paul and Long,[1] it depends upon the " salting in " effect of the large organic molecules or ions upon the basic form of the indicator.

Methanesulphonic acid behaves as a much stronger acid than any of the others investigated here, though its solutions are less acidic than those of hydrochloric, perchloric, sulphuric, or nitric acids. It has been recently shown [3] that the acidity functions of the strong acids can be accounted for quantitatively up to about 8M by a simple treatment involving the assumption that the hydrogen ion in aqueous solution is firmly associated with four water molecules. If we assume that the same treatment can be applied to methanesulphonic acid, then by inserting the observed values of H_0 in eqn. (5) of ref. 3, it is possible to compute the true hydrogen-ion concentration and hence the degree of dissociation. This gives 89%, 86%, 64%, and 53% dissociation at 0·5, 1·0, 2·0, and 3·0M, corresponding to a concentration dissociation constant of about 4: *i.e.*, methane sulphonic acid is intermediate in strength between trifluoroacetic acid ($K = 0{\cdot}18$) and nitric acid ($K = 23$).[19]

The validity of this procedure can be tested by using it to calculate the acidity functions of aqueous nitric acid, for which the true degrees of dissociation are known with some certainty from measurements of Raman spectra and proton magnetic resonance.[19] The results of such calculations are shown in Table 12: the agreement is as good as could be expected.

TABLE 12. *Observed and calculated acidity functions for aqueous nitric acid.*

Concn.	2·00	3·54	4·55	5·61	6·74
a	0·95	0·89	0·84	0·76	0·71
H_0 calc.	−0·66	−1·21	−1·51	−1·79	−2·10
H_0 obs.	−0·67	−1·18	−1·47	−1·71	−1·94

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* The values given by Bell and Brown [15] for potassium hydrogen sulphate indicate a levelling off of the acidity at a relatively low value in the range 1—3M, but recent and more accurate measurements by Satchell [18] show that it does in fact behave like the other inorganic acids.

[18] Satchell, *J.*, 1958, 3904.

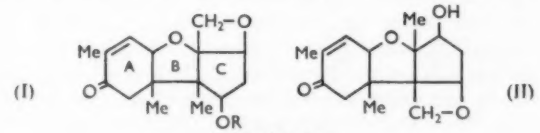
[19] Young, Wu, and Krawetz, *Discuss. Faraday Soc.*, 1957, **24**, 37 and personal communication from Professor Young.

224. *The Structure of Trichothecin and its Hydrolysis Products.*

By G. G. Freeman, J. E. Gill, and W. S. Waring.

Trichothecin is the *iso*crotonic ester of the ketonic alcohol, trichothecolone. On the basis of its properties and those of degradation products, obtained by oxidation, alkaline fission, and dehydrogenation, the alternative structures (I; R=H) and (II), of which the former is preferred, are proposed for trichothecolone. On treatment with hot potassium hydroxide, trichothecolone gives an isomer, *iso*trichothecolone. Some properties and derivatives of the latter are described.

Trichothecin is an antifungal substance, produced by the fungus *Trichothecium roseum* Link.[1] Some of its chemical and biological properties have been described.[2-4] It is an ester, $C_{19}H_{24}O_5$, giving [5] on hydrolysis *iso*crotonic acid and a ketonic alcohol, trichothecolone, $C_{15}H_{20}O_4$. Trichothecin was readily hydrogenated at atmospheric pressure with palladium–charcoal, two mols. of hydrogen being absorbed to give the non-crystalline tetrahydrotrichothecin. This uptake was accounted for by saturation of one ethylenic double bond in the *iso*crotonic ester group and a second ethylenic double bond in the trichothecolone part of the molecule. Trichothecin contained a reactive carbonyl group, which was retained in tetrahydrotrichothecin. Kuhn–Roth determinations showed that trichothecin has at least three *C*-methyl groups. No methoxyl group was detected. The infrared spectrum of trichothecin had bands at 1670 (αβ-unsaturated ketone), 1710 and 1177 (αβ-unsaturated ester), and 1650 cm.$^{-1}$ (attributed to ethylenic unsaturation). Absence of a band in the region of 3400 cm.$^{-1}$ indicated absence of hydroxyl groups which was confirmed by indifference of trichothecin, even under the most vigorous conditions, to acetic anhydride or benzoyl chloride. There was no indication of benzenoid absorption in the spectrum.



Trichothecolone when R = H

Trichothecin was readily hydrolysed with cold methanolic potassium hydroxide to trichothecolone (98% yield) and β-methoxybutyric acid (presumably formed by addition of methanol to *iso*crotonic acid; Purdie and Marshall [6] showed that ethyl crotonate on treatment with sodium methoxide gave sodium β-methoxybutyrate). Hydrolysis of trichothecin with boiling aqueous 0·5N-sodium hydroxide gave *iso*crotonic acid and *iso*trichothecolone, isomeric with trichothecolone. The functional groups of trichothecin (I; R = CHMe:CH·CO) were thus shown to be two ethylenic double bonds, a ketonic group, and an ester group, which account for three of the five oxygen atoms in the molecule.

Trichothecin reacted exothermally with concentrated hydrochloric acid to form a chlorohydrin $C_{19}H_{25}O_5Cl$, m. p. 132·5°; the infrared spectrum of this showed a band associated with a hydroxyl group whose presence was confirmed by quantitative acetylation though the acetyl derivative of the chlorohydrin was not obtained crystalline. The chlorohydrin was still ketonic. Hydrolysis of this chlorohydrin with methanolic potassium hydroxide at room temperature gave trichothecolone chlorohydrin (III), m. p. 139—140°, also formed by the action of 10N-hydrochloric acid on trichothecolone. This indicated that

[1] Freeman and Morrison, *Nature*, 1948, **162**, 30.
[2] *Idem, Biochem. J.*, 1949, **44**, 1.
[3] *Idem, J. Gen. Microbiol.*, 1949, **3**, 60.
[4] Freeman, *ibid.*, 1955, **12**, 213.
[5] Freeman and Gill, *Nature*, 1950, **166**, 698.
[6] Purdie and Marshall, *J.*, 1891, 468.

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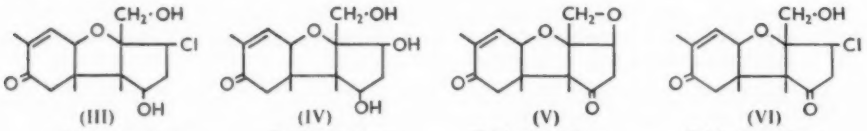
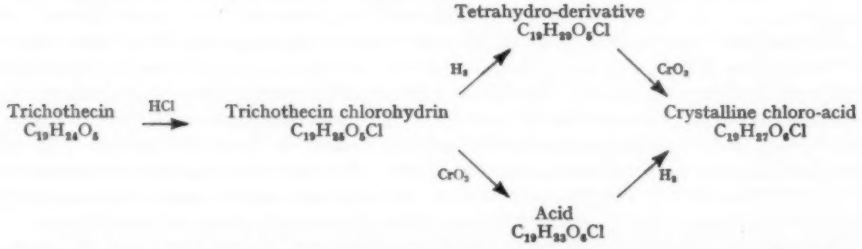
the hydrochloric acid had reacted with the trichothecolone part of the molecule, opening an ether linkage with formation of an alcoholic group. Trichothecin chlorohydrin was not formed when dry hydrogen chloride was passed into solutions of trichothecin in ether or chloroform, and trichothecin did not produce hydroxyl ions when warmed with sodium thiosulphate in 50% acetone,[7] which are normal reactions of epoxides. Trichothecin bromohydrin $C_{19}H_{25}O_5Br$ and trichothecolone bromohydrin $C_{15}H_{21}O_4Br$ were prepared in analogous ways.



Trichothecolone chlorohydrin — Trichothecolone glycol — Trichothecodione — Trichothecodione chlorohydrin

When trichothecin was boiled in 0·1N-hydrochloric acid, addition of water took place, giving a glycol, $C_{19}H_{26}O_6$, hydrolysed by cold alkali to trichothecolone glycol (IV), which was also obtained from trichothecolone. Quantitative acetylation indicated that there were three hydroxyl groups present in trichothecolone glycol and it is assumed that two of these have been formed by opening of an oxygen ring. Trichothecolone glycol adsorbed one mol. of hydrogen at ordinary temperature to form dihydrotrichothecolone glycol which was also prepared by the action of boiling 0·5N-sulphuric acid on dihydrotrichothecolone. Trichothecolone glycol was recovered unchanged after one hour's boiling in 15% aqueous potassium hydroxide. Acetylation of trichothecolone glycol gave a non-crystalline triacetyl derivative. The glycols from trichothecin and trichothecolone were both ketonic.

Hydrogenation of trichothecin chlorohydrin at ordinary pressure gave the non-crystalline tetrahydrotrichothecin chlorohydrin which on oxidation with chromic acid gave a chloro-acid, $C_{19}H_{27}O_6Cl$, with no loss of carbon. The chloro-acid no longer contained a hydroxyl group, but was still ketonic, formed an amide, and sublimed *in vacuo* unchanged. Oxidation of trichothecin chlorohydrin with chromic acid gave an acid, $C_{19}H_{23}O_6Cl$, which on hydrogenation gave the crystalline chloro-acid, $C_{19}H_{27}O_6Cl$, described above.



In a similar way, trichothecin bromohydrin was hydrogenated to non-crystalline tetrahydrotrichothecin bromohydrin, and this was oxidised to the corresponding saturated bromo-acid, $C_{19}H_{27}O_6Br$. These reactions with concentrated hydrochloric and hydrobromic acid can be explained by assuming that trichothecin contained an oxide ring which was easily opened by strong acids with the formation of a hydroxymethyl group. Oxidation of the latter then resulted in the formation of a carboxylic acid with no loss of carbon. Tetrahydrotrichothecin also reacted with concentrated hydrochloric acid. Cold alkaline hydrolysis of the saturated chloro-acid $C_{19}H_{27}O_6Cl$ gave a hydroxy-chloro-acid, m. p. 199°, $C_{15}H_{21}O_5Cl$.

Trichothecolone.—The keto-alcohol trichothecolone, $C_{15}H_{20}O_4$, contains at least two

[7] Ross, *J.*, 1950, 2257.

C-methyl groups (Kuhn–Roth) and one active hydrogen (hydroxyl group). Its infrared spectrum has bands at 1650 (C:C), 1670 (C:C·CO) and 3510 cm.$^{-1}$ (OH) but no benzenoid absorption. Its carbonyl group is reactive (semicarbazone; deep orange 2 : 4-dinitrophenylhydrazone). It readily gave an acetyl derivative, which formed a 2 : 4-dinitrophenylhydrazone and regenerated trichothecolone on hydrolysis at room temperature. The infrared spectrum of acetyltrichothecolone contained no OH band, indicating that normal esterification had occurred. Cold alkaline hydrolysis of trichothecin 2 : 4-dinitrophenylhydrazone yielded trichothecolone 2 : 4-dinitrophenylhydrazone, identical with that prepared from the alcohol.

In presence of palladium–charcoal trichothecolone rapidly absorbed one mol. of hydrogen, the product still being ketonic (semicarbazone and 2 : 4-dinitrophenylhydrazone). The ease of hydrogenation precluded hydrogenolysis and this was supported by the formation of acetyldihydrotrichothecolone (no infrared OH band). The wave number of the carbonyl group in the infrared spectrum of dihydrotrichothecolone was 1695 cm.$^{-1}$ and that of trichothecolone was 1670 cm.$^{-1}$, the change indicating loss of αβ-conjugation. As described below, a similar difference was observed for the six-membered ring ketonic groups of trichothecodione and dihydrotrichothecodione. The ultraviolet absorptions of trichothecin, trichothecolone, and *iso*trichothecolone (see Table), when compared with Woodward's [8] observations on αβ-unsaturated ketones [monosubstituted (α or β) 2250 ± 50 Å; disubstituted (αβ or ββ) 2390 Å; trisubstituted (αββ) 2540 Å], suggest that trichothecolone and *iso*trichothecolone are α- or β-monosubstituted αβ-unsaturated ketones. Hydrogenation caused the disappearance of the bands, *e.g.*, tetrahydrotrichothecin and dihydrotrichothecolone showed no high-intensity absorption. In the spectrum of trichothecolone semicarbazone there was a displacement of the band to longer wavelength (by 410 Å) and an increase in intensity (by ε 12,000). This behaviour was characteristic of αβ-unsaturated ketones.[9]

	$\lambda_{max.}$ (Å)	ε	$\lambda_{max.}$ (Å)	ε
	In hexane		In MeOH	
Trichothecin	2170	18,000	2150	19,000
Trichothecolone	2240	8000	2260	8000
*iso*Trichothecolone	2220	9000	2300	8050

A number of esters of trichothecolone was prepared by treating the alcohol with the acid anhydrides in pyridine, but *iso*crotonyltrichothecolone was not obtained. Some biological properties of these esters have been reported.[4] Hydrogenation of butyryltrichothecolone gave an oil, presumed to be butyryldihydrotrichothecolone, which formed a microcrystalline semicarbazone identical with that prepared from the non-crystalline tetrahydrotrichothecin.

Trichothecolone gave a negative result in the haloform reaction, indicating the absence of the CH_3·CO group. Both trichothecolone and *iso*trichothecolone reacted as primary and secondary alcohols with nitric–chromic acid reagent [10] which did not distinguish between the two compounds. Trichothecolone did not react with phthalic anhydride in benzene or toluene, as expected of a primary alcohol. Ozonolysis of trichothecolone in chloroform gave acetic acid (0·58 mol. by titration; isolated as *p*-phenylphenacyl acetate) and acetaldehyde but no other characterisable products. Oxidations of trichothecolone, *iso*trichothecolone, or dihydrotrichothecolone with potassium permanganate gave only water-soluble products, including oxalic acid. Oxidation of tetrahydrotrichothecodiol with potassium permanganate gave 0·95 mol. of acetic acid.

Oxidation Products of Trichothecolone.—Oxidation of trichothecolone and dihydrotrichothecolone with chromic acid gave compounds containing two hydrogen atoms less. The product, trichothecodione (V), from the former gave a mono-semicarbazone, a mono-2 : 4-dinitrophenylhydrazone, and in small yield a bis-2 : 4-dinitrophenylhydrazone.

[8] Woodward, *J. Amer. Chem. Soc.*, 1941, **63**, 1123.
[9] Evans and Gillam, *J.*, 1943, 565.
[10] Fearon and Mitchell, *Analyst*, 1932, **57**, 372.

Dihydrotrichothecolone gave on oxidation dihydrotrichothecodione which formed a mono-2 : 4-dinitrophenylhydrazone, and was also prepared by hydrogenation of trichothecodione. The infrared spectra of these diones did not contain the hydroxyl band (3510 cm.$^{-1}$) of trichothecolone. The bands at 1670 cm.$^{-1}$ for trichothecodione and at 1710 cm.$^{-1}$ for dihydrotrichothecodione, attributed to the original ketonic group, were present, together with a new band at 1735 cm.$^{-1}$ due to a new carbonyl. This was consistent with the presence of a secondary alcoholic group in trichothecolone and its dihydro-derivative. The difference in frequency between the two carbonyl groups in trichothecodione indicated that the hydroxyl group in trichothecolone was not attached to the same ring as the carbonyl group. The frequency of the carbonyl group at 1735 cm.$^{-1}$ is of the order of that of an unconjugated, five-membered ring ketone.

The second carbonyl group in trichothecodione was relatively unreactive to ketonic reagents. The ultraviolet absorption showed a maximum at 2250 Å (ε 8600) and its semicarbazone a maximum at 2680 Å (ε 21,700), characteristic of an $\alpha\beta$-unsaturated ketone, and this suggested that the original carbonyl of trichothecolone was the more reactive one in trichothecodione. Trichothecodione did not give a pyrrole derivative on reaction with ammonia, a colour with ferric chloride, or a copper complex. Thus the characteristic reactions of $\alpha\beta$- and $\alpha\gamma$-diketones were absent.

Trichothecodione with cold 10N-hydrochloric acid yielded a chlorohydrin (VI) in a way analogous to that of trichothecin, so the oxide bridge is intact in the dione. The chlorohydrin was ketonic. Similarly dihydrotrichothecodione in 10N-hydrochloric acid formed a crystalline chlorohydrin in 34% yield. Trichothecolone chlorohydrin with aqueous chromic acid gave trichothecodione chlorohydrin, which was isolated as the dinitrophenylhydrazone.

Oxidation of the hydroxy-chloro-acid $C_{15}H_{21}O_5Cl$ (see above) of dihydrotrichothecodione chlorohydrin, and of dihydrotrichothecolone chlorohydrin with chromic acid, each gave a product, $C_{15}H_{18}O_5$ (XIX), isolated as 2 : 4-dinitrophenylhydrazones which were shown to be identical by mixed m. p. and comparison of their *X*-ray powder photographs.

Dehydrogenation of Tetrahydrotrichothecodiol.—As a preliminary to dehydrogenation, trichothecolone was hydrogenated at 100°/100 atm. in the presence of Raney nickel. The colourless amorphous product, tetrahydrotrichothecodiol $C_{15}H_{26}O_4$, did not react with Brady's reagent and carbonyl absorption was absent from its infrared spectrum. Tetrahydrotrichothecodiol has three active hydrogen atoms and analysis of its acetyl derivative indicated the presence of three acetyl groups, although the results were not conclusive. These observations suggested that hydrogenolysis had occurred. Estimation of the *C*-methyl content gave a slightly higher value than that obtained for trichothecolone.

Tetrahydrotrichothecodiol was unchanged by palladium–charcoal in boiling 1-methylnaphthalene for 6 hr. but in absence of solvent decomposition commenced at 140°. The volatile products were collected by distillation up to 300°. Further decomposition products were obtained by distillation when the residue was heated *in vacuo*, and by extracting the residue with solvents, respectively. The products consisted of water (2·75 mols.), *p*-xylene, and two ketones, $C_7H_{10}O$ and $C_7H_{12}O$. Reduction of a mixture of the ketones gave a saturated ketone $C_5H_6Me_2O$, which did not form a dibenzylidene derivative and hence was not 3 : 4-dimethyl*cyclo*pentanone; its 2 : 4-dinitrophenylhydrazone and semicarbazone were identical with those of 2 : 3-dimethyl*cyclo*pentanone (mixed m. p.; infrared spectrum). 2 : 4-, 3 : 4-, and 2 : 5-Dimethyl*cyclo*pentanone were prepared and gave different 2 : 4-dinitrophenylhydrazones.

2 : 3-Dimethyl*cyclo*pent-2-enone [11] gave a semicarbazone and 2 : 4-dinitrophenylhydrazone identical with those of our ketone $C_7H_{10}O$. The absorption maximum of authentic 2 : 3-dimethyl*cyclo*pent-2-enone was at 2335 $\pm$ 10 Å; that of the degradation product (2290 $\pm$ 10 Å) may have been shifted by impurities.

[11] Frank, Armstrong, Kwiatek, and Price, *J. Amer. Chem. Soc.*, 1948, **70**, 1379.

XUM

The oil which was obtained by solvent extraction of the residue from the dehydrogenation was separated into two fractions by steam-distillation. The infrared spectrum of the steam-volatile fraction indicated hydroxyl, carbonyl, and ethylenic groups. Fractionation by distillation gave *p*-xylenol. Attempts to aromatise the higher-boiling fraction by bromination and dehydrobromination, and by dehydrogenation, gave a compound which still contained traces of hydroxyl and carbonyl groups but was probably identical with or very similar to the product (described below) obtained by reduction of dihydrotrichothecolone with phosphorus and hydriodic acid.

The following observations are of importance in interpretation of the dehydrogenation experiments: (1) The reaction was carried out under relatively mild conditions; although the temperature was finally raised to 300°, the bulk of the product distilled at 140—220°. (2) The yields of *p*-xylene and 2 : 3-dimethyl*cyclo*pentanone were such that their formation by breakdown of a single ring cannot be excluded. (3) The infrared spectrum of trichothecodione indicates the presence of a *cyclo*pentanone nucleus. (4) The bulk of the oxygen in the starting material was accounted for by formation of approximately three mols. of water and of the *cyclo*pentanones. (5) The fifteen carbon atoms of tetrahydrotrichothecodiol were accounted for on a qualitative, though not a quantitative basis, by those present in the products (*p*-xylene and dimethyl*cyclo*pentanone). (6) Tetrahydrotrichothecodiol probably contained three *C*-methyl groups (Found: 13·0. Required for 3*C*-Me, 16·7%), whereas the dehydrogenation products contained four *C*-methyl groups. Taken as a whole this evidence strongly suggests that the precursors of *p*-xylene and of 2 : 3-dimethyl*cyclo*pentanone exist as independent rings in tetrahydrotrichothecodiol and that a five-membered carbon ring, substituted by a hydroxyl group (in tetrahydrotrichothecodiol) and a keto-group (in trichothecodione), gives rise to the *cyclo*pentanone isolated.

Dehydration-dehydrogenation of *cyclo*hexanol has been reported to occur in the presence of various catalysts such as platinum,[12] nickel–aluminium, rhenium, silica gel,[13] and copper chromite [14] with production of benzene, phenol, and *cyclo*hexanone. Analogous reactions leading to *p*-xylene and *p*-xylenol from a substituted *cyclo*hexanol system seem probable in the dehydrogenation of tetrahydrotrichothecodiol. The position of the carbonyl band in the infrared spectrum of trichothecolone (1670 cm.$^{-1}$) indicates that it is present in a six-membered ring; isolation of *p*-xylenol from the dehydrogenation of tetrahydrotrichothecodiol furnishes supporting evidence of the presence of a C_6 ring in the latter compound. The low temperature of the reaction precludes isomerisation of the methyl groups, and this is supported by the isolation of pure *p*-xylene; a mixture of xylenes would be expected if isomerisation had occurred.

High-pressure hydrogenation of trichothecolone glycol and dehydrogenation of the product, under the conditions used for tetrahydrotrichothecodiol, also gave *p*-xylene, 2 : 3-dimethyl*cyclo*pentanone, and 2 : 3-dimethyl*cyclo*pent-2-enone. *p*-Xylene and the same *cyclo*pentenone were also isolated by dehydrogenation of the hydrogenated neutral compound (VII) obtained by oxidation of trichothecolone glycol with aqueous chromic acid (see below). High-pressure hydrogenation of an acid (XX) prepared by oxidation of the primary alcohol group in *neo*trichothecodione (see below) and hydrogenation of the ethylenic bonds, followed by the usual dehydrogenation, further gave *p*-xylenol and 2-methyl*cyclo*pentanone after hydrogenation of a ketonic mixture (cf. Scheme 3): isolation of 2-methyl*cyclo*pentanone in this experiment supports the interpretation (below) that the methylene group of the methyleneoxy-bridge in trichothecolone is in the β-position with respect to the hydroxyl group, and appears as the 3-methyl group in 2 : 3-dimethyl-*cyclo*pentanone. The carboxyl group of the acid (XX) is assumed to have been lost by decarboxylation under the conditions of the experiment. Dehydrogenation of the product of high-pressure hydrogenation of the saturated acid (XI) occurred only at a very high

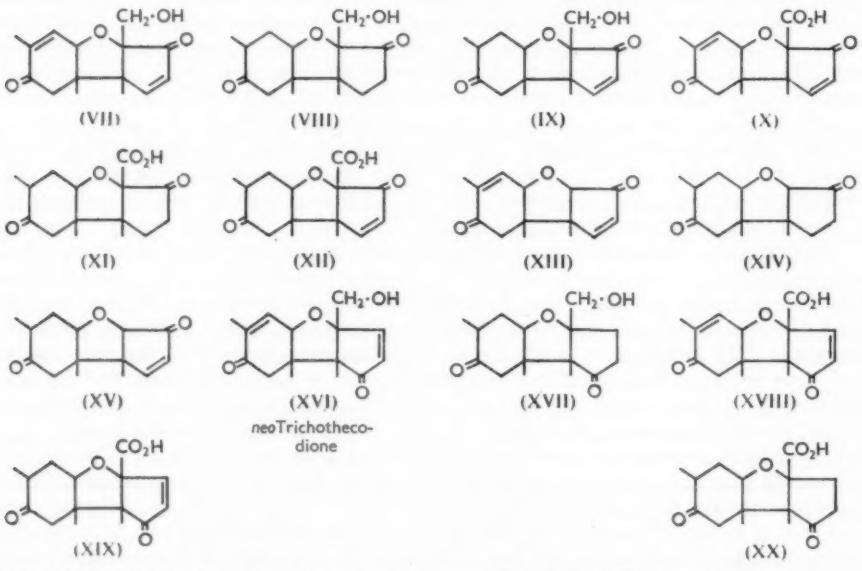
[12] Adkins, Richards, and Davis, *ibid.*, 1941, **63**, 1320.
[13] Rollett and Maurer-Stroh, *Ber.*, 1940, **73**, 740.
[14] Hurd, Greengard, and Roe, *J. Amer. Chem. Soc.*, 1939, **61**, 3359.

XUM

temperature; *p*-xylenol and a mixture of 2- with some 3-methyl*cyclo*pentanone were obtained after hydrogenation at atmospheric pressure.

Alkaline Fission of Trichothecodione.—When trichothecodione was heated for 3 min. with one equivalent of sodium hydroxide *neo*trichothecodione (XVI) (see below) was isolated (62% yield). Boiling for 2 min. with an excess of 10% sodium hydroxide solution gave *p*-xyloquinone (10—15%) and *p*-xyloquinol (25%) (under similar conditions it was found that about 90% of authentic *p*-xyloquinone was irrecoverable). These products were consistent with the hypothesis that trichothecolone contains a six-membered ring having two methyl groups or potential methyl groups in the *para*-position to each other and also two oxygen atoms in the *para*-position to each other. Dehydrogenation and infrared evidence suggested that one of these oxygen atoms was in the form of a keto-group. Certain other derivatives of trichothecin gave small amounts of *p*-xyloquinone when heated with an excess of sodium hydroxide, *e.g.*, trichothecin chlorohydrin (5%), *neo*-trichothecodione (5%), the chloro-acid $C_{19}H_{27}O_6Cl$ (8%), and the acid (XVIII) (6%) (see below). The formation of *p*-xyloquinone from the latter acid confirmed the findings and was in agreement with the deductions drawn from the dehydrogenation of acid (XX), *viz.*, that the methyleneoxy-bridge was attached to that part of the molecule which gave rise to 2 : 3-dimethyl*cyclo*pentanone. No quinone was detected when acid (X) or ketone (XIII) was heated with aqueous sodium hydroxide. The acid (XX), $C_{15}H_{16}O_5$, decomposed in hot dilute sodium hydroxide solution giving a compound $C_8H_{12}O_2$. This product gave slight reduction of Tollens's reagent at room temperature. A purer specimen, free from reducing properties towards Tollens's reagent, has since been obtained by other workers.[15]

Further C_{15} *and* C_{14} *Oxidation Products of Trichothecolone Derivatives.*—Oxidation of trichothecolone glycol (IV) with aqueous chromic acid at room temperature gave a neutral compound (VII) (42% yield), $\lambda_{max.}$ 2270 Å (ε 13,500), $\nu_{max.}$ 3440 (OH) and 1710 and 1680 cm.$^{-1}$



(both >CO), which formed an orange mono-2 : 4-dinitrophenylhydrazone and a mono-acetate. The acetate showed no infrared hydroxyl band but an ester group and two bands at 1680 cm.$^{-1}$ and 1750 cm.$^{-1}$ and regenerated the compound (VII) on alkaline hydrolysis in good yield. On hydrogenation in the presence of palladium–charcoal

[15] Fishman, Jones, and Whiting, personal communication, 1957.

compound (VII) absorbed two mols. of hydrogen, giving a compound (VIII), which formed a yellow mono-2 : 4-dinitrophenylhydrazone. When dihydrotrichothecolone glycol was oxidised with aqueous chromic acid an unsaturated diketone (IX) was obtained, having an ultraviolet absorption maximum at 2190 Å (ε 6250), forming an orange mono-2 : 4-dinitrophenylhydrazone, and giving on hydrogenation the ketone (VIII).

Formation of compound (VII) by aqueous chromic acid from trichothecolone glycol (IV) may be explained on the basis of (*a*) oxidation, to a keto-group, of the secondary hydroxyl group formed in ring C by addition of water to trichothecolone, and (*b*) loss of water from the αβ-position to the new ketonic group. Quantitative acetylation of trichothecolone glycol indicated the presence of three hydroxyl groups whereas acetylation of compound (VII) showed only one hydroxyl group per molecule. The hydrogenation of compound (VII) to (VIII), and the increased intensity in the ultraviolet absorption spectrum of (VII), suggest that a new ethylenic link has been formed during oxidation, probably in conjugation with the new carbonyl group. This is supported by the formation of compound (IX) on oxidation of dihydrotrichothecolone glycol. The facts that compound (IX) can be hydrogenated to (VIII) and that the former shows definite ultraviolet absorption whereas dihydrotrichothecolone glycol has no high-intensity absorption are further evidence in favour of new unsaturation. The three neutral compounds (VII, VIII, IX) were oxidised to acids by the action of chromic acid in acetic acid. Oxidation of the compound $C_{15}H_{18}O_4$ (VII) gave the acid $C_{15}H_{16}O_5$ (X) (obtained as a monohydrate). Its ultraviolet absorption showed a maximum at 2270 Å (ε 12,500). Oxidation of the compound (VIII) $C_{15}H_{22}O_4$ gave the acid $C_{15}H_{20}O_5$ (XI), and of the compound (IX) $C_{15}H_{20}O_4$ gave the acid $C_{15}H_{18}O_5$ (XII).

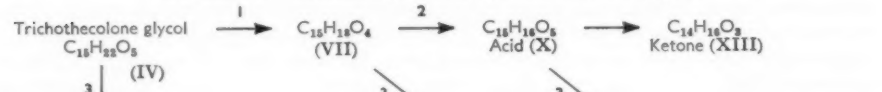
The acid-catalysed opening of the oxygen bridge in trichothecin has been shown to give rise to a primary hydroxyl group which is present in trichothecolone glycol (IV) and in (VII, VIII, and IX). Although stable to cold aqueous chromic acid the primary hydroxyl group is attacked by chromic acid in acetic acid (a very much faster reaction than in water; cf. Cohen and Westheimer [16]) with the formation of acids (X, XI, and XII). These three acids lost carbon dioxide on melting and gave crystalline neutral ketones. Acid (X) gave the ketone $C_{14}H_{16}O_3$ (XIII); acid (XI) gave the ketone $C_{14}H_{20}O_3$ (XIV); and acid $C_{15}H_{18}O_5$ (XII) gave the ketone $C_{14}H_{18}O_3$ (XV). The behaviour of the acids on melting was suggestive of β-keto-acids. Their failure to react with aqueous ferric chloride suggests that they may be αα-disubstituted β-keto-acids. The semicarbazone of ketone (XIV) crystallised from chloroform, and apparently held solvent of crystallisation; the analytical figures agreed better with those for the bis- than the mono-derivative. The dinitrophenylhydrazone of (XIV) also gave analytical figures in closer agreement with those for a bis- than a mono-derivative. The inter-relationship of the acids and ketones from trichothecolone is summarised in Scheme 1.

Isomers of Trichothecodione and Dihydrotrichothecodione.—When trichothecodione (V) was warmed with ammonia or sodium carbonate solution, or with one equivalent of sodium hydroxide for a short time, isomerisation occurred yielding *neo*trichothecodione (XVI). Similarly, dihydrotrichothecodione yielded *neo*dihydrotrichothecodione. Both *neo*-compounds gave mono-2 : 4-dinitrophenylhydrazones. It seemed probable that the isomerism involved the opening of a methyleneoxy-bridge and the elimination of an oxygen atom from the β-position to a carbonyl group. In support of this it was found that *neo*trichothecodione contained a hydroxyl group (as shown by quantitative acetylation and infrared absorption spectrum). The infrared spectra of these compounds showed strong absorption due to a hydroxyl group, and to ketonic bands at 1700 cm.$^{-1}$ and 1720 cm.$^{-1}$ respectively. *neo*Trichothecodione was found to possess two ethylenic double bonds, and *neo*dihydrotrichothecodione one such bond, by quantitative hydrogenation, both giving the same compound (XVII), $C_{15}H_{22}O_4$, thus confirming the presence of a new ethylenic bond in these two compounds. The intensity of the ultraviolet absorption of

[16] Cohen and Westheimer, *J. Amer. Chem. Soc.*, 1952, **74**, 4387.

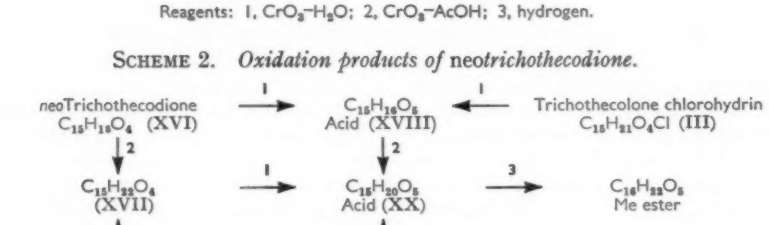
*neo*trichothecodione ($\lambda_{max.}$ 2200 Å, ε 12,910) was almost double that of trichothecodione ($\lambda_{max.}$ 2250 Å, ε 8600), which indicated that the new ethylenic bond in *neo*trichothecodione was conjugated with a keto-group. In further support of the hypothesis, *neo*trichothecodione contained a new hydroxyl group, being oxidised by chromic acid to an acid (XVIII), $C_{15}H_{16}O_5$ (Scheme 2). Similarly *neo*dihydrotrichothecodione was oxidised to an acid (XIX), $C_{15}H_{18}O_5$. These acids were hydrogenated to the same saturated acid (XX),

SCHEME 1. *Oxidation products of trichothecolone glycol.*



Reagents: 1, CrO_3–H_2O; 2, CrO_3–AcOH; 3, hydrogen.

SCHEME 2. *Oxidation products of* neo*trichothecodione.*



Reagents: 1, CrO_3; 2, hydrogen; 3, CH_2N_2.

$C_{15}H_{20}O_5$, proving that a new ethylenic double bond had been introduced during the isomerisation of trichothecodione. Oxidation of the compound (XVII) with chromic acid gave the acid (XX). The acids (XVIII—XX) were not decarboxylated on melting, and thus differed from those obtained from the trichothecolone glycol series. The β-elimination of water involved when the methyleneoxy-bridge was opened during the alkaline isomerisation of trichothecodione, was paralleled by the β-elimination of hydrogen chloride from trichothecolone chlorohydrin (in which the methyleneoxy-bridge was already open) when this was oxidised with chromic acid. The products of oxidation of the chlorohydrins were identical with those obtained from the corresponding derivatives in the *neo*trichothecodione series. Thus oxidation of trichothecolone chlorohydrin (III) yielded acid (XVIII), and oxidation of dihydrotrichothecolone chlorohydrin yielded acid (XIX). Both these acids were hydrogenated to acid (XX), identical with that obtained from the *neo*trichothecodione series. Acid (XIX) gave an orange 2 : 4-dinitrophenylhydrazone, and acid (XX) gave a crystalline methyl ester.

Tests for an Oxide Ring.—According to their rate of liberation of hydroxyl ions in the presence of sodium thiosulphate (cf. Ross [7]), trichothecin and its derivatives may be divided into three classes. Trichothecolone, dihydrotrichothecolone, trichothecodione, dihydrotrichothecodione, *neo*trichothecodione, and *neo*dihydrotrichothecodione gave typical rapid, positive reactions, indicative of the presence of an oxide ring. In the case of trichothecolone, when the pink colour of phenolphthalein was continuously discharged

with acetic acid, 0·52 equivalent of labile oxygen was accounted for in 7 hours' heating. Compounds of the second group slowly developed weak pink colours; these included acetyltrichothecolone, butyryltrichothecolone, *iso*trichothecolone, trichothecolone glycol, and trichothecolone chlorohydrin. Negative reactions were given by trichothecin, trichothecin glycol, trichothecin chlorohydrin, crotonyltrichothecolone, and acid (XI). Comparative experiments with reference compounds containing 3—6-membered oxide rings are detailed on p. 1128.

The negative reaction obtained with trichothecin may be explained by its ease of hydrolysis with alkali, so that the liberated hydroxyl ions reacted with the ester group and never reached a sufficiently high concentration to be detected by the indicator. Support for this view is afforded by glycidyl acetate whose normal strongly positive reaction is suppressed by the presence of methyl oxalate (cold) or ethyl acetate (on warming). The strongly positive reactions of *neo*trichothecodione (XVI) and *neo*dihydrotrichothecodione, in which the methyleneoxy-bridge is absent, may be due to the presence of a *cyclo*pentenone system. The same explanation is suggested for the weakly positive reaction of compound (VII), which contains a different *cyclo*pentenone structure.

According to Nicholson [17] the ring strain associated with five-, four-, and three-membered saturated rings containing one oxygen atom is 6, 22, and 27 kcal. mole^{-1}, respectively (corresponding figures for carbon rings are 6, 26, and 27 kcal. mole^{-1}). Although not enough compounds have been examined to make it clear how far these values are constant, the heat of reaction of trichothecolone and hydrochloric acid was determined to provide some evidence of the nature of the oxygen ring in this compound. In case the bond reaction was not exactly neutral the reaction of epichlorohydrin with hydrochloric acid was examined: the heat of reaction in this case (29 kcal. mole^{-1}) was in agreement with the above generalisation. In duplicate experiments the heat of reaction of trichothecolone with hydrochloric acid was found to be (sample 1) 26·5, 28·9, (sample 2) 23·2, 22·9 kcal. mole^{-1}. This did not distinguish between a three- and a four-membered ring for trichothecolone but the structure appeared to contain one or the other. That the result for trichothecolone is lower than for epichlorohydrin suggests that a four-membered ring is present.

Miscellaneous Reactions of Trichothecolone and its Derivatives.—A small yield of *p*-xyloquinone was obtained when trichothecolone was boiled with aqueous chromic acid.

Boiling hydriodic acid and red phosphorus converted dihydrotrichothecolone into a liquid, b. p. 230—240°, $n_D^{21·5}$ 1·5252, and a similar product was obtained by dehydrogenation of tetrahydrotrichothecodiol. The properties of these products were in reasonable agreement with those of a hydrocarbon, $C_{15}H_{28}$, which showed no aromatic absorption in its infrared spectrum.

None of the compounds of the trichothecin or trichothecolone series gave normal αβ-glycol reactions with periodate. Trichothecolone glycol was, however, slowly oxidised to compound (VII).

Trichothecodione and *neo*trichothecodione both reduced Fehling's solution and Tollens's reagent.

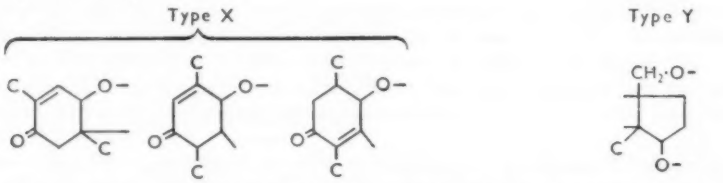
Structure of Trichothecolone.—The infrared spectrum of trichothecolone (band at 1670 cm.$^{-1}$) shows the presence of an αβ-unsaturated ketone group in a six-membered ring, and the ultraviolet spectrum (max. at 2260 Å, ε 8000) conforms to this type with either 0 or 1 alkyl substituent on the ethylenic bond and an oxygen atom attached to the γ-carbon atom. Trichothecolone is a secondary alcohol which on oxidation gives trichothecodione having a new, relatively unreactive carbonyl group (1735 cm.$^{-1}$) in a different ring from the other; so the original ketonic and hydroxyl groups of trichothecolone are in different rings. Trichothecin contains an easily opened oxygen bridge, giving with concentrated hydrochloric acid a chlorohydrin which contains a new hydroxyl group that is oxidised to an acid without loss of carbon. The bridge is therefore a methyleneoxy-bridge,

[17] Nicholson, personal communication, 1952.

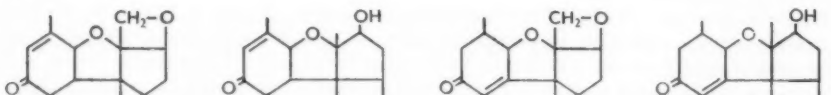
XUM

$-CH_2 \cdot O- \longrightarrow -CH_2 \cdot OH\ Cl-$. Three of the oxygen atoms of trichothecolone are thus accounted for. The fourth is assumed to be in an ether group. The action of hot dilute acids on trichothecolone opens the methyleneoxy-bridge with addition of water and gives trichothecolone glycol ($-CH_2 \cdot O- \longrightarrow -CH_2 \cdot OH\ HO-$), which is oxidised in stages and, without loss of carbon, gives rise to acids which are decarboxylated at their m. p.s. Dilute alkali isomerises trichothecodione to *neo*trichothecodione in which a new hydroxyl group and ethylenic double bond are present. This isomerism is interpreted as a β-elimination of the oxygen atom of the methyleneoxy-bridge, after opening of this ring. Oxidation of *neo*trichothecodione gives, with no loss of carbon, a series of acids, identical with those obtained by oxidation of the trichothecolone chlorohydrin series.

Dehydrogenation of fully reduced trichothecolone gave *p*-xylene, *p*-xylenol, 2 : 3-dimethyl*cyclo*pentanone, and 2 : 3-dimethyl*cyclo*pent-2-enone. The action of hot alkali on trichothecodione yielded *p*-xyloquinone and *p*-xyloquinol; *p*-xyloquinone was obtained by oxidation of trichothecolone with hot chromic acid. It thus seems probable that the keto-group in trichothecolone is present in a *cyclo*hex-2-enone ring to which are attached two methyl groups or potential methyl groups in the *para*-position to each other, and an oxygen atom also *para* to the ketonic group. Dehydrogenation of acid (XX), which had been obtained by opening the oxygen bridge in trichothecolone (either *via* trichothecolone chlorohydrin or *neo*trichothecodione), and oxidation of the primary alcoholic group so formed to carboxyl, gave not 2 : 3-dimethyl*cyclo*pentanone, but 2-methyl*cyclo*pentanone together with *p*-xylenol: isolation of 2-methyl*cyclo*pentanone in this experiment supports the interpretation that the methylene group of the methyleneoxy-bridge is in the β-position with respect to the hydroxyl group. The carboxyl group of acid (XX) is assumed to have been lost by decarboxylation.



The degradation fragments can thus be arranged to conform to the skeletal types (X) and (Y).* These two together comprise all the carbon and oxygen atoms in trichothecolone; suitable junctions of them yield six possible structural formulæ, (I; R = H), (II), (IA and B), (IIA and B), for trichothecolone. Of these, formula (I) is preferred for the following reasons.

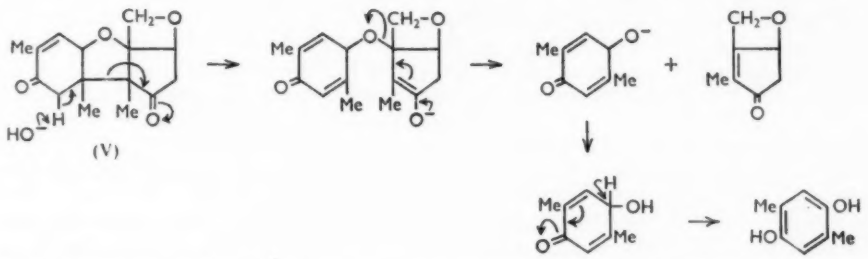


That tetrahydrotrichothecolone with potassium permanganate gave 0·95 mol. of acetic acid is in better agreement with formulæ (I) and (II) than with the other four. Substances (IA and B) and (IIA and B) would be expected to yield a fifteen-carbon compound containing an aromatic six-membered ring on mild dehydrogenation, yet this did not occur when trichothecolone derivatives were treated with hydriodic acid, and this is further evidence in favour of formulæ (I) and (II), with a quaternary carbon atom in the six-membered ring.

The easy breakdown of trichothecodione by alkali, involving rupture of a C–C bond, is almost certainly due to alkaline cleavage of a 1 : 5-diketone, followed by β-elimination of the substituted alkoxy-group, the mechanism being as in the annexed formulæ. The

* We are indebted to a Referee for constructive help in elucidation of various possibilities.

four-membered oxide ring may be opened before, during, or after the 1 : 5-cleavage, but this would not affect the formation of *p*-xyloquinol. The trichothecodione corresponding to (IA) would also be a 1 : 5-diketone and alkaline cleavage should likewise yield *p*-xyloquinol. On the other hand, the trichothecodione from (IB) would contain a vinylogous



(V)

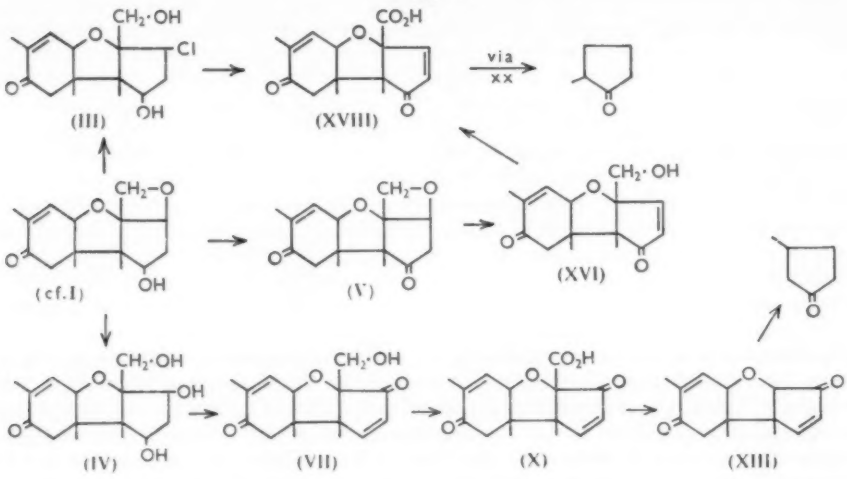
1 : 3-diketone system and would probably not undergo alkaline cleavage at room temperature. Structure (IB) can also be excluded because it should absorb at about 2480 Å (cf. Dorfman [18]), whereas the observed absorption in methanol is at 2260 Å (the calculated value on the same basis is 2300 Å). The trichothecodiones corresponding to (II) and (IIA) contain 1 : 6-diketone systems, and that from (IIB) contains the vinylogue of a 1 : 4-diketone system. Compounds with the structures (IA) and (IIA) would be expected to be readily converted, probably by aerial oxidation under alkaline conditions, into a C_{15} phenol: this reaction has never been observed with trichothecolone derivatives. Structures (IB) and (IIB) have highly substituted ethylenic double bonds, which might be expected to undergo hydrogenation only with difficulty, whereas trichothecolone and its derivatives were readily hydrogenated. Thus, only structure (I) is left in agreement with all the facts.

The difference in properties between the trichothecolone chlorohydrin and the trichothecolone glycol series is believed to depend upon the oxidation of different hydroxyl groups in the two series. Trichothecolone glycol gives a series of acids which are decarboxylated on melting, whereas trichothecolone chlorohydrin gives a different series which are not decarboxylated on melting but are identical with the acids obtained in the *neo*trichothecodione series. On dehydrogenation, acid (XX) (derived from the trichothecolone chlorohydrin series) gave 2-methyl*cyclo*pentanone presumably by the route shown in Scheme 3. Under similar conditions, the acid (XI) (from trichothecolone glycol) would be expected to yield 3-methyl*cyclo*pentanone (cf. Scheme 3). Dehydrogenation of this acid, however, required the high temperature of 350° and yielded a mixture of 2- and 3-methyl*cyclo*pentanone. Since our experimental work was completed, Fishman, Jones, and Whiting [15] have accumulated evidence based on alkaline fission of diketonic derivatives into C_7 and C_8 fragments, that confirms the structures of the acids and ketones derived from trichothecolone glycol and chlorohydrin, respectively, on the basis of formula (I). They have also confirmed the view that different hydroxyl groups are involved in the oxidation of trichothecolone chlorohydrin and of trichothecolone glycol (cf. Scheme 3).

iso*Trichothecolone.*—*iso*Trichothecolone is obtained by isomerisation of trichothecolone or directly from trichothecin with hot caustic alkali. It contains at least two *C*-methyl groups but two active hydrogen atoms. A hydroxyl group is denoted by an infrared band at 3400 cm.$^{-1}$ (cf. trichothecolone, 3510 cm.$^{-1}$; see Figure). It forms a mono-2 : 4-dinitrophenylhydrazone and a mono-*p*-nitrobenzoate, m. p. 195—196°. It is indifferent to concentrated hydrochloric acid (or hot 30% aqueous sodium hydroxide), which suggests that the methyleneoxy-bridge is absent in *iso*trichothecolone and is involved in the isomerisation of trichothecolone to *iso*trichothecolone. In an attempt to dehydrate *iso*trichothecolone with phosphorus oxychloride in pyridine a phosphorus-containing

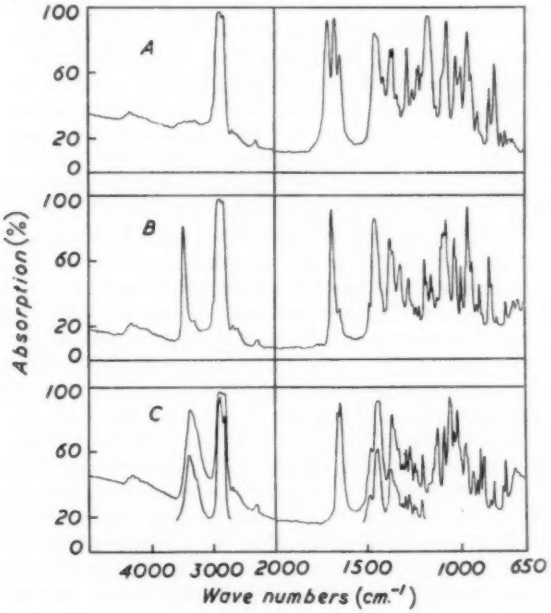
[18] Dorfman, *Chem. Rev.*, 1953, **53**, 73.

SCHEME 3. *Routes to ketonic dehydrogenation products from trichothecolone chlorohydrin and glycol.*



crystalline product, $C_{15}H_{18}O_5PCl$, was obtained, whose infrared spectrum showed the absence of hydroxyl groups, but a ketonic band at 1667 cm.$^{-1}$.

Infrared spectra of trichothecin (*A*), *trichothecolone* (*B*), *and* iso*trichothecolone* (*C*) (*solids, mulled*).



In the presence of palladium-charcoal, *iso*trichothecolone at atmospheric pressure very rapidly absorbed one mol. of hydrogen, giving dihydro*iso*trichothecolone (which is

dimorphic), identical with that obtained by alkaline isomerisation of dihydrotrichothecolone. Thus *iso*trichothecolone retains the ethylenic bond of trichothecolone, which is not concerned in or necessary to the conversion of trichothecolone into its isomeride.

*iso*Trichothecolone formed a monoacetyl derivative when heated with an excess of acetic anhydride in pyridine or with glacial acetic acid alone, and hydrolysis of this acetyl derivative regenerated *iso*trichothecolone. A different acetylation product, obtained by means of acetic anhydride and sodium acetate, has been shown at Oxford [15] to be a diacetate. Monoacetyl*iso*trichothecolone absorbs 1 mol. of hydrogen (palladium–charcoal), the product giving dihydro*iso*trichothecolone on hydrolysis and being obtained also by acetylation of dihydro*iso*trichothecolone.

Oxidation Products of iso*Trichothecolone.*—Oxidation of *iso*trichothecolone with aqueous chromic acid at room temperature gave *iso*trichothecodione having infrared bands at 3390 (OH), 1667 (original >CO), and 1721 cm.$^{-1}$ (new >CO). This dione was unchanged by cold 10N-hydrochloric acid or boiling 2N-sulphuric acid, and on hydrogenation (palladium–charcoal) gave dihydro*iso*trichothecodione [infrared band at 3400 (OH) and 1706 cm.$^{-1}$ (>CO)]. Oxidation of dihydro*iso*trichothecolone with aqueous chromic acid at room temperature gave an acid $C_{15}H_{22}O_7$, which was not decarboxylated on melting and this acid was obtained also from dihydro*iso*trichothecodione by chromic acid in acetic acid.

The isomerisation of trichothecolone to *iso*trichothecolone clearly involves the methyleneoxy-group and the range of structural possibilities is limited by the experiments described above. The present evidence is, however, insufficient for proposal of a final structural formula for *iso*trichothecolone.

Experimental

Trichothecin was prepared as described by Freeman and Morrison.[2] Analytical work was carried out by Drs. Weiler and Strauss, and in the Analytical Laboratories of the Dyestuffs and Nobel Divisions of Imperial Chemical Industries Limited. The infrared spectra of solid specimens, in " Nujol " between rock-salt plates, were measured in the double-beam recording infrared spectrometer described by Tetlow *et al.*[19] The bulk of this work was done in 1949—53 and some of the observations, including those reproduced as the Figure, were recently confirmed by measurements in a Hilger H800 recording double-beam infrared spectrometer. Owing to the variations in the thickness of the specimens used, it was not possible to compare the intensities in the spectrum of one compound with those of another. Cells, constructed from rock-salt plates, were used for liquid specimens.

Trichothecin gave *C*-Me values 13·8, 14·4, 13·1% (Calc. for $C_{19}H_{24}O_5$: 3-*C*Me, 13·5%. Other analytical data have been reported [5]) and $\lambda_{max.}$ 2170 Å (ε 18,000) in hexane. The *semicarbazone*, crystallised from methanol or aqueous methanol, had m. p. 243—244° (decomp.) (Found: C, 61·3; H, 7·0; N, 11·3. $C_{20}H_{27}O_5N_3$ requires C, 61·7; H, 6·9; N, 10·8%).

10N-Hydrochloric acid (0·15 ml.) was added to trichothecin (0·15 g.) and 2 : 4-dinitrophenylhydrazine (0·1 g.) in boiling ethanol (7·5 ml.). The 2 : 4-*dinitrophenylhydrazone* crystallised from ethanol as pale orange-coloured needles (0·15 g.), m. p. 203° (corr.) (Found: C, 58·6, 58·7; H, 5·2, 5·2; N, 10·5, 10·8. $C_{25}H_{28}O_8N_4$ requires C, 58·6; H, 5·5; N, 10·9%).

Hydrolysis of Trichothecin 2 : 4-*Dinitrophenylhydrazone.*—Trichothecin 2 : 4-dinitrophenylhydrazone (0·4 g.), in methanolic N-potassium hydroxide (16 ml.), was set aside at room temperature for 17 hr. The methanol was removed *in vacuo* and the dark brown residue extracted with chloroform. The solvent was removed and the residue crystallised from ethanol as deep orange rods (0·37 g.), m. p. 263—265° (corr.) alone or mixed with trichothecolone 2 : 4-dinitrophenylhydrazone (see below).

Tetrahydrotrichothecin.—Trichothecin (0·5 g.) in methanol at 22° in the presence of palladium–charcoal absorbed 78 ml. of hydrogen ($2H_2$ = 68 ml. at N.T.P.). Removal of the catalyst and distillation of the methanol *in vacuo* left the product as a colourless syrup.

This tetrahydrotrichothecin (0·18 g.) gave the *semicarbazone* (0·2 g.), m. p. 220° (decomp.), as a thick gel from methanol (Found: C, 60·2, 60·1; H, 7·85, 7·8; N, 10·95, 10·7. $C_{20}H_{31}O_5N_3$ requires C 61·1; H 7·9; N 10·7%); $\lambda_{max.}$ in methanol, 2280 Å (ε 14,000).

Trichothecolone.—Trichothecin (1·0 g.) in cold methanolic N-potassium hydroxide (40 ml.)

[19] Tetlow, McAuslan, Brimley, and Price, *J. Sci. Instr.*, 1951, **28**, 161.

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was kept at room temperature for 17 hr. Water (30 ml.) was added and the methanol removed under reduced pressure below 35°. The aqueous residue was extracted with chloroform. Removal of the chloroform left colourless *trichothecolone* (0·776 g.), which crystallised from benzene–light petroleum (2 : 1) in long colourless needles, m. p. 183—184° (corr.) soluble in water and most organic solvents except light petroleum [Found: C, 67·9, 68·8, 68·9; H, 7·5, 7·3, 7·3; *C*-Me 10·6 10·0; active H, 0·47; *M* (Rast), 244, 248. $C_{15}H_{20}O_4$ requires C, 68·2; H, 7·6; 2*C*-Me, 11·4; 1 active H, 0·37%; *M*, 264], $[\alpha]_D^{19·5}$ +22·5° (*c* 1 in chloroform), $[\alpha]_D^{18}$ +17° (*c* 1 in ethanol), $\lambda_{max.}$ (in methanol), 2260 Å (ε 8000). The chlororm-extracted aqueous solution was acidified with sulphuric acid and extracted with chloroform, evaporation of which left colourless liquid β-methoxybutyric acid (0·26 g.) (Freeman and Gill [5]).

Acetic anhydride (2 ml.) and trichothecolone (0·25 g.) in pyridine (3 ml.) gave, in 4 days at room temperature, the *acetyl derivative* as prisms (0·274 g.) (from methanol), m. p. 148—149° (corr.) (Found: C, 66·4; H, 7·0; Ac, 19·8. $C_{17}H_{22}O_5$ requires C, 66·7; H, 7·2; 1Ac, 14·1%), $\lambda_{max.}$ 2270 Å (ε 8000) in MeOH.

Acetyltrichothecolone (0·3 g.), on hydrolysis with methanolic potassium hydroxide, gave trichothecolone (0·23 g.).

Trichothecolone 2 : 4-*dinitrophenylhydrazone* was prepared by Brady and Elsmie's method [20] and crystallised from chloroform–ethanol (1 : 3) as deep orange rods, m. p. 261—262° (corr.) (Found: C, 56·2; H, 5·6; N, 11·9, 11·9. $C_{21}H_{24}O_7N_4$ requires C, 56·7; H, 5·4; N, 12·6%).

Acetyltrichothecolone 2 : 4-*dinitrophenylhydrazone* crystallised from chloroform–ethanol (1 : 3) as orange needles, m. p. 251—252° (corr.) (Found: C, 56·2, 56·5; H, 5·3, 5·2; N, 12·0, 11·8; Ac, 19·3. $C_{23}H_{26}O_8N_4$ requires C, 56·8; H, 5·3; N, 11·5; 1Ac, 8·9%).

Trichothecolone (0·264 g.) gave a *semicarbazone* (0·341 g.), m. p. 250—251°, colourless needles from methanol (Found: C, 59·4; H, 7·25; N, 12·9. $C_{16}H_{23}O_4N_3$ requires C, 59·8; H, 7·2; N, 13·1%), $\lambda_{max.}$ (in methanol), 2670 Å (ε 20,000).

Dihydrotrichothecolone.—Hydrogenation of trichothecolone (3·0 g.) at atmospheric pressure led to uptake of one mol. of hydrogen. *Dihydrotrichothecolone* crystallised from benzene–light petroleum (1 : 1) as colourless rods (2·65 g.), m. p. 178—179° (corr.) (Found: C, 67·5, 67·6; H, 8·0, 8·3. $C_{15}H_{22}O_4$ requires C, 67·7; H, 8·3%), identical with a specimen prepared by hydrolysis of tetrahydrotrichothecin.[5]

Dihydrotrichothecolone 2 : 4-dinitrophenylhydrazone crystallised from ethanol as orange needles, m. p. 170—171° (corr.). The *semicarbazone*, prepared by the usual method, crystallised as needles (from methanol), m. p. 258—259° (decomp.) (Found: C, 59·5; H, 7·5; N, 13·25. $C_{16}H_{25}O_4N_3$ requires C, 59·4; H, 7·7; N, 13·0%), $\lambda_{max.}$ (in methanol) 2290 Å (ε 13,000).

Dihydrotrichothecolone (0·2 g.) was acetylated by pyridine–acetic anhydride, and *acetyldihydrotrichothecolone* crystallised from toluene–light petroleum (1 : 1) as prisms (0·19 g.), m. p. 126·5—127·5° (corr.) (Found: C, 66·0; H, 8·0; Ac, 14·5. $C_{17}H_{24}O_5$ requires C, 66·2; H, 7·9; 1Ac, 14·0%).

Butyryltrichothecolone.—To a solution of trichothecolone (0·264 g.) in dry pyridine (3 ml.), cooled in ice, was added butyric anhydride (2 ml.). The *ester* (0·21 g.) crystallised from aqueous methanol as prisms, m. p. 105—106° (Found: C, 68·25; H, 7·5. $C_{19}H_{26}O_5$ requires C, 68·3; H, 7·8%), $\lambda_{max.}$ 2220 Å (ε 8000) in hexane.

Hydrogenation. Butyryltrichothecolone (0·11 g.) in methanol was shaken with hydrogen in the presence of Adams catalyst for 1 hr. The oily product (butyryldihydrotrichothecolone) was converted into the *semicarbazone* which separated from hot methanol as a gelatinous mass (0·125 g.), m. p. 220° (decomp.) (Found: C, 61·2; H, 7·75; N, 11·1. $C_{20}H_{31}O_5N_3$ requires C 61·1; H, 7·9; N, 10·7%). *X*-Ray powder photographs of this and tetrahydrotrichothecin semicarbazone showed them both to be microcrystalline and identical.

Crotonyltrichothecolone.—Trichothecolone (0·264 g.) was treated with pyridine (3 ml.) and crotonic anhydride (2 ml.). The sticky *ester* (0·372 g.), after being washed with light petroleum (b. p. 40—60°), crystallised from methanol in cream-coloured needles (0·142 g.), m. p. 117—118° (Found: C, 68·3; H, 7·0. $C_{19}H_{24}O_5$ requires C, 68·7; H, 7·2%), $\lambda_{max.}$ 2170 Å (ε 11,000) in hexane.

Ozonolysis of Trichothecolone.—Ozonised oxygen was passed into a solution of trichothecolone (0·25 g.) in dry chloroform (20 ml.) for 4 hr. at 0°. Removal of the solvent under reduced pressure left a colourless amorphous residue which was treated with water (25 ml.) at room temperature for 20 hr. The aqueous solution was distilled. A portion of the distillate, treated

[20] Brady and Elsmie, *Analyst*, 1926, **51**, 77.

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with Brady's reagent, gave a small precipitate of acetaldehyde-2 : 4-dinitrophenylhydrazone, m. p. 142—144°, undepressed on admixture with an authentic specimen (m. p. 148—149°). The acidity of the distillate was equivalent to 0·58 mol. of acid, and the acid was identified as its *p*-phenylphenacyl ester, m. p. 108·5—110°, undepressed on admixture with *p*-phenylphenacyl acetate.

Trichothecodione.—A 5% solution of chromic anhydride in 95% acetic acid (40 ml.) was added to trichothecolone (2·0 g.) in glacial acetic acid (5 ml.). A slight initial rise in temperature was controlled by cooling in ice-water, and the mixture was then set aside for 1 hr. Pouring it into cold water (200 ml.) gave crystalline *trichothecodione*. This recrystallised from aqueous ethanol as colourless rods (1·45 g.), m. p. 218—219° (corr.) [Found: C, 69·0; H, 7·0%; *M* (Rast), 232, 244. $C_{15}H_{18}O_4$ requires C, 68·7; H, 6·9%; *M*, 262], readily soluble in most solvents except water and light petroleum.

The dione (0·1 g.) was treated in ethanol (1 ml.) with Brady's reagent (70 ml.). The 2 : 4-*dinitrophenylhydrazone* crystallised from ethanol as deep orange plates (0·13 g.), m. p. 220—221° (corr.) (Found: C, 57·6, 57·2; H, 5·1, 4·9; N, 12·3, 12·4. $C_{21}H_{22}O_7N_4$ requires C, 57·0; H, 5·0; N, 12·7%). A second preparation by this method gave a *form* (orange plates), m. p. 143° (corr.). On further heating this resolidified and melted at 220—221° (Found: C, 56·7; H, 5·1; N, 12·6, 13·0%). The infrared spectra of the two hydrazones were identical; they showed a band at 1740 cm.$^{-1}$, whilst the band at 1670 cm.$^{-1}$ was absent, indicating that the 2 : 4-dinitrophenylhydrazine had reacted with the original ketonic group. The lower-melting compound is believed to be am etastable form.

Trichothecodione (1·0 g.) was boiled with 2 : 4-dinitrophenylhydrazine (1·5 g.) in ethanol (50 ml.) and 10N-hydrochloric acid (1·5 ml.) for 2 hr. A reddish-brown precipitate (0·946 g.) was filtered off from the boiling solution, and had m. p. 212°. Extraction of this product with boiling ethanol and chloroform left a red solid which was insoluble in all common solvents, except acetone. It was extracted with boiling acetone, and the solution concentrated to crystallisation, to obtain a deep red *bis*-2 : 4-*dinitrophenylhydrazone* (0·025 g.), which darkened at 200° but did not melt below 300° (Found: C, 47·6; H, 3·5; N, 20·2; Cl, 0. $C_{27}H_{26}O_{10}N_8$ requires C, 52·1; H, 4·2; N, 18·0%).

The *monosemicarbazone* crystallised from aqueous methanol and had m. p. 227° (decomp.) (Found: C, 59·9; H, 6·5; N, 13·0. $C_{16}H_{21}O_4N_3$ requires C, 60·2; H, 6·6; N, 13·2%), $\lambda_{max.}$ (in methanol), 2680 Å (ε 21,700).

Dihydrotrichothecodione.—(*a*) Oxidation of dihydrotrichothecolone (2·5 g.) with chromic acid in acetic acid gave colourless rods of *dihydrotrichothecodione* (1·97 g.) (from aqueous ethanol), m. p. 164—164·5° (corr.) (Found: C, 68·3, 68·0; H, 7·5, 7·5. $C_{15}H_{20}O_4$ requires C, 68·2; H, 7·6%).

(*b*) Trichothecodione (0·25 g.) in ethanol (50 ml.) was hydrogenated at atmospheric pressure with 10% palladium–charcoal (0·2 g.). The theoretical quantity of hydrogen was absorbed in 30 minutes, giving crystals (0·245 g.), m. p. 161—162° undepressed on admixture with the preceding material.

Dihydrotrichothecodione mono-2 : 4-dinitrophenylhydrazone crystallised from ethanol as yellow needles, m. p. 225—226° (corr.) (Found: C, 56·9, 56·5; H, 5·5, 5·4; N, 12·8, 13·3. $C_{21}H_{24}O_7N_4$ requires C, 56·8; H, 5·4; N, 12·6%).

Trichothecin Chlorohydrin.—Trichothecin (0·25 g.) was triturated with 10N-hydrochloric acid (2·5 ml.), and ethanol (1 ml.) added to obtain complete solution. On stirring, the *chlorohydrin* crystallised. It recrystallised from dilute acetic acid as colourless rods (0·183 g.), m. p. 132·5° (corr.) (Found: C, 61·8; H, 6·8; Cl, 9·4; active H, 0·43. $C_{19}H_{25}O_5Cl$ requires C, 61·9; H, 6·8; Cl, 9·6; 1 active H, 0·33%). Quantitative acetylation indicated the presence of one hydroxyl group per molecule, and the infrared spectrum confirmed the presence of carbonyl, ester, and hydroxyl groups. This compound was not obtained by passing dry hydrogen chloride into a solution of trichothecin in dry ether or chloroform.

The acetyl derivative of trichothecin chlorohydrin was amorphous and melted at 43—53° (Found: C, 59·7; H, 7·1; Cl, 9·8; Ac, 14·3. Calc. for $C_{21}H_{27}O_6Cl$: C, 61·4; H, 6·3; Cl, 8·9; Ac, 10·5%). *Trichothecin chlorohydrin* 2 : 4-*dinitrophenylhydrazone* was obtained as orange crystals, m. p. 205° (corr.) (Found: C, 54·4; H, 5·2; N, 10·9. $C_{25}H_{29}O_9N_4Cl$ requires C, 54·7; H, 5·3; N, 10·7%). *Trichothecin chlorohydrin* 4-*chloro*-2-*nitrophenylhydrazone* crystallised from acetic acid as bright red needles, m. p. 187—188° (Found: C, 55·5; H, 5·3; N, 7·4. $C_{25}H_{29}O_6N_3Cl_2$ requires C, 55·8; H, 5·4; N, 7·8%).

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Tetrahydrotrichothecin Chlorohydrin.—Trichothecin chlorohydrin (0·184 g.) in methanol was shaken with hydrogen in the presence of palladium–charcoal. 2 Mols. of hydrogen were absorbed in 5 min. The tetrahydro-derivative was isolated as a glass (0·145 g.).

Reduction of Trichothecin Chlorohydrin with Zinc and Acetic Acid.—Trichothecin chlorohydrin (0·3 g.) in glacial acetic acid (15 ml.) and zinc dust (0·9 g.) were heated on the water-bath for 7 hr. The *product* crystallised from methanol as colourless needles (0·047 g.), m. p. 166—167° (Found: C, 61·8; H, 7·2; Cl, 9·2. $C_{19}H_{27}O_5Cl$ requires C, 61·5; H, 7·3; Cl, 9·6%). The infrared absorption spectrum showed no carbonyl band, but bands due to hydroxyl and ester were present.

Trichothecolone Chlorohydrin.—(*a*) *By hydrolysis of trichothecin chlorohydrin.* Hydrolysis of trichothecin chlorohydrin (0·726 g.) with methanolic potassium hydroxide gave *trichothecolone chlorohydrin* (0·70 g.) as colourless needles (from ether), m. p. 139—140° (corr.) (Found: C, 60·2, 60·0; H, 7·2, 7·0; Cl, 11·7. $C_{15}H_{21}O_4Cl$ requires C, 59·9; H, 7·0; Cl, 11·8%). The liquid acid (0·097 g.), b. p. 210°, present in the aqueous alkaline fraction was isolated as *p*-phenylphenacyl β-methoxybutyrate, m. p. 60° (cf. Drake and Bronitsky [21]).

(*b*) *By reaction of trichothecolone with aqueous hydrochloric acid.* Trichothecolone (2 g.) dissolved rapidly in 10N-hydrochloric acid (2 ml.) with evolution of heat. The residue obtained by evaporation crystallised from benzene–light petroleum (1 : 1) as needles, m. p. 133—134° (corr.) undepressed on admixture with the chlorohydrin described above.

Trichothecolone chlorohydrin (0·3 g.) gave the *semicarbazone* (0·254 g.) as prisms (from methanol), m. p. 214° (decomp.) (Found: C, 52·4; H, 6·5; N, 11·5. $C_{15}H_{24}O_4N_3Cl$ requires C, 52·1; H, 6·9; N, 12·1%). The 2 : 4-*dinitrophenylhydrazone* was prepared by Brady's method and crystallised from methanol in orange-red crystals, m. p. 278—279° (decomp.) (Found: C, 52·3; H, 5·3; N, 11·8; Cl, 6·6. $C_{21}H_{25}O_7N_4Cl$ requires C, 52·5; H, 5·2; N, 11·7; Cl, 7·4%). The 4-*chloro*-2-*nitrophenylhydrazone* crystallised from acetic acid in short red-brown prisms, m. p. 242—243° (decomp.) (Found: C, 53·9; H, 5·5; N, 8·0. $C_{21}H_{25}O_5N_3Cl_2$ requires C, 53·6; H, 5·3; N, 8·9%), and the 4-*bromo*-2-*nitrophenylhydrazone* from acetic acid as orange prisms, m. p. 231—232° (decomp.) (Found: C, 49·4; H, 4·9; N, 7·8. $C_{21}H_{25}O_5N_3ClBr$ requires C, 49·0; H, 4·9; N, 8·2%).

Hydrogenation of Trichothecolone Chlorohydrin.—Trichothecolone chlorohydrin (0·25 g.) in ethanol (20 ml.) was hydrogenated at atmospheric pressure in the presence of Adams catalyst (0·2 g.). Reduction was rapid, the total uptake of hydrogen being 60 ml. (N.T.P.) ($2H_2$ = 37 ml.). The product (0·251 g.) separated from benzene–light petroleum (1 : 1) as a white amorphous solid (0·192 g.), m. p. 164—165° (corr.). It gave no reaction with Brady's reagent.

Trichothecin Bromohydrin.—Trichothecin (0·5 g.) and concentrated hydrobromic acid (5 ml.) gave colourless needles of *trichothecin bromohydrin* (0·45 g.), m. p. 140°, from dilute acetic acid (Found: C, 53·6; H, 5·9. $C_{19}H_{25}O_5Br$ requires C, 55·2; H, 6·0%). The corresponding tetrahydro-derivative was a thick gum.

Trichothecolone Bromohydrin.—Hydrolysis of trichothecin bromohydrin (1·0 g.) gave *trichothecolone bromohydrin* (0·9 g.), needles (from benzene), m. p. 129—130° (Found: C, 52·5; H, 6·1. $C_{15}H_{21}O_4Br$ requires C, 52·2; H, 6·1%). This gave a *semicarbazone*, prisms (from aqueous methanol), darkening at 240° without melting (Found: C, 46·6; H, 5·9; N, 10·4. $C_{15}H_{24}O_4N_3Br$ requires C, 46·2; H, 6·2; N, 10·8%), and a 4-*chloro*-2-*nitrophenylhydrazone*, brown-red prisms (from acetic acid), m. p. 226—227° (decomp.) (Found: C, 48·7; H, 4·8; N, 8·1. $C_{21}H_{25}O_5N_3ClBr$ requires C, 49·0; H, 4·9; N, 8·2%).

Trichothecin Glycol.—A solution of trichothecin (0·635 g.) in 0·1N-hydrochloric acid (1500 ml.) was heated at 100° for 2 hr. The hydrochloric acid was neutralised to pH 6·0 by 2N-sodium hydroxide, and the solution concentrated to 130 ml. under reduced pressure. *Trichothecin glycol* crystallised as colourless prisms (0·374 g.), m. p. 146·5° (corr.) [Found: C, 64·9, 65·1; H, 7·5, 7·4%; *M* (Rast), 338, 330. $C_{19}H_{26}O_6$ requires C, 65·1; H, 7·4%; *M*, 350]. This formed a 2 : 4-*dinitrophenylhydrazone* by Brady's method, which crystallised from aqueous alcohol in reddish-orange rods, m. p. 216° (corr.) (Found: C, 56·8, 56·7; H, 5·6, 5·5; N, 9·9, 9·7. $C_{25}H_{30}O_9N_4$ requires C, 56·6; H, 5·7; N, 10·6%).

Trichothecolone Glycol.—(a) *From trichothecin glycol.* Hydrolysis of trichothecin glycol (4·23 g.) with methanolic potassium hydroxide gave colourless prisms, m. p. 193—194° (corr.), (3·15 g.) from acetone. The m. p. of the product was undepressed on admixture with trichothecolone glycol (m. p. 193°) prepared as in (b).

[21] Drake and Bronitsky, *J. Amer. Chem. Soc.*, 1930, **52**, 3715.

(b) *From trichothecolone.* Trichothecolone (5·0 g.) in 0·5N-sulphuric acid (500 ml.) was heated under reflux for 2 hr. The solution was cooled and made neutral to Congo Red by barium carbonate (60 g.). The filtrate was evaporated to dryness and the residue crystallised from ethanol as colourless prismatic crystals of *trichothecolone glycol* (4·3 g.), m. p. 193—194° (corr.) [Found: C, 63·5; H, 7·8; *C*-Me, 12·0%; *M* (Rast), 310, 305. $C_{15}H_{22}O_5$ requires C, 63·8; H, 7·8; 3*C*-Me, 15·9%; *M*, 282], $\lambda_{max.}$ (in methanol) 2260 Å (ε 6500).

(c) Trichothecolone glycol was also prepared by treatment of trichothecolone with 50% (w/w) sulphuric acid at room temperature for 24 hr.

The pale red *glycol* 2 : 4-*dinitrophenylhydrazone* crystallised from ethanol; at 189° it softened and changed crystalline form to long needles which melted at 273° (corr.) (Found: C, 54·3, 54·6; H, 5·7, 5·6; N, 12·2, 12·3. $C_{21}H_{26}O_8N_4$ requires C, 54·5; H, 5·6; N, 12·1%).

Trichothecolone glycol (0·1 g.) with acetic anhydride–pyridine gave a syrupy *triacetate* (0·135 g.) (Found: C, 61·6, 61·8; H, 7·5, 7·3; Ac, 33·3. $C_{21}H_{28}O_8$ requires C, 61·7; H, 6·9; 3Ac, 31·6%).

Dihydrotrichothecolone Glycol.—(*a*) Trichothecolone glycol (0·5 g.) in ethanol (12 ml.) was hydrogenated at atmospheric pressure with palladium–charcoal as catalyst. The product (0·5 g.) crystallised from ethanol in colourless prisms, m. p. 216—217°.

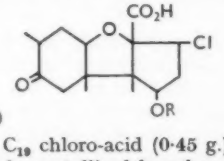
(*b*) Dihydrotrichothecolone (1·0 g.) in 0·5N-sulphuric acid (100 ml.) was heated under reflux for 2 hr. and gave the *glycol* (0·72 g.) which, crystallised from ethanol, had m. p. 215° (Found: C, 63·2, 63·3; H, 8·5, 8·5. $C_{15}H_{24}O_5$ requires C, 63·4; H, 8·5%).

Reaction of Trichothecodione with Acids: Trichothecodione Chlorohydrin.—Trichothecodione (0·45 g.) was triturated with concentrated hydrochloric acid (5 ml.), and the *chlorohydrin* precipitated from the solution by dilution with water (25 ml.). Recrystallisation from ethanol gave colourless, rectangular prisms (0·204 g.), m. p. 165° (corr.) (Found: C, 60·3; H, 6·4; Cl, 11·4. $C_{15}H_{19}O_4Cl$ requires C, 60·3; H, 6·4; Cl, 11·9%). Its 2 : 4-*dinitrophenylhydrazone* crystallised from ethanol as orange needles, m. p. 213° (decomp.) (corr.) (Found: C, 52·5; H, 5·1; N, 11·6; Cl, 7·3. $C_{21}H_{23}O_7N_4Cl$ requires C, 52·7; H, 4·8; N, 11·7; Cl, 7·4%). An identical hydrazone was obtained by oxidation of trichothecolone chlorohydrin (0·5 g.) with 5% aqueous chromic acid (10 ml.).

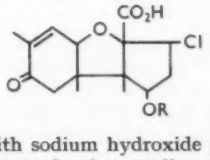
Dihydrotrichothecodione Chlorohydrin.—Dihydrotrichothecodione (0·5 g.) reacted similarly with acid, to give the *chlorohydrin* (0·195 g.), m. p. 174—176° (decomp.) (corr.) (Found: C, 60·4; H, 7·2; Cl, 10·8. $C_{15}H_{21}O_4Cl$ requires C, 59·9; H, 7·0; Cl, 11·8%).

Oxidation of Trichothecin Halogenohydrins to Acids.—(a) *Tetrahydrotrichothecin chlorohydrin.* Tetrahydrotrichothecin chlorohydrin (1·0 g.) was dissolved in glacial acetic acid (5 ml.) and the solution divided into 5 equal parts. Each aliquot part (1 ml.) was treated with 5% chromic acid in glacial acetic acid (6 ml.) and the temperature allowed to rise to 32°. After 1 hr. the combined solutions were poured into water (200 ml.) and extracted with chloroform. The chloroform solution was extracted with sodium hydrogen carbonate solution, and acidification of the alkaline extract precipitated an *acid* (XXI; R = Pr·CO) which crystallised from aqueous methanol in colourless needles (0·574 g.), m. p. 171—172° (Found: C, 59·5, 59·1, 59·0; H, 7·1, 7·2, 7·0; Cl, 9·4, 9·2%; equiv., 398. $C_{19}H_{27}O_6Cl$ requires C, 59·0; H, 7·0; Cl, 9·2%; equiv., 386·5). The acid gave no colour with ferric chloride, absorbed no hydrogen in the presence of palladium–charcoal, and had no high-intensity absorption. It gave a 2 : 4-*dinitrophenylhydrazone* as bright yellow prisms, m. p. 125°, from benzene (Found: C, 52·6; H, 5·2; N, 9·6. $C_{25}H_{31}O_9N_4Cl$ requires C, 52·9; H, 5·5; N, 9·9%).

The C_{19} chloro-acid (0·055 g.) was heated in thionyl chloride (1 ml.) at 80° for 30 min. Excess of thionyl chloride was removed *in vacuo*, and the residue dissolved in ether and treated with dry ammonia. The *amide* (0·045 g.) crystallised from aqueous methanol in prisms (0·016 g.), m. p. 165—166° (Found: N, 3·3. $C_{19}H_{28}O_5NCl$ requires N, 3·6%).



(XXI)



(XXII)

Hydrolysis of the C_{19} chloro-acid (0·45 g.) with sodium hydroxide gave a C_{15} *acid* (XXI; R = H) (0·388 g.) which crystallised from benzene as colourless needles, m. p. 198—199° (Found, after drying at 130°: C, 57·8; H, 7·0; Cl, 9·9. $C_{15}H_{21}O_5Cl$ requires C, 56·9; H, 6·6; Cl, 11·2%).

(b) *Trichothecin chlorohydrin.* In a similar way trichothecin chlorohydrin (0·2 g.) was

oxidised with chromic acid in acetic acid and gave an *acid* (XXII; R = CHMe·CH·CO) (0·115 g.), m. p. 85—90° (Found: C, 58·3; H, 6·2; Cl, 9·8%; equiv., 389. $C_{19}H_{23}O_6Cl$ requires C, 59·6; H, 6·0; Cl, 9·3%; equiv., 382·5). The acid (0·115 g.) was hydrogenated at atmospheric pressure in the presence of palladium–charcoal, giving colourless needles (0·082 g.), m. p. 169—170°, of acid (XXI; R = Pr·CO).

(c) *Tetrahydrotrichothecin bromohydrin.* Similarly, tetrahydrotrichothecin bromohydrin (0·24 g.) gave a C_{19} *bromo-acid* (0·125 g.) as colourless needles (from aqueous methanol), m. p. 176—177° (Found: C, 52·9; H, 5·9. $C_{19}H_{27}O_6Br$ requires C, 52·9; H, 6·3%).

Tetrahydrotrichothecodiol.—Trichothecolone (4·0 g.) in absolute ethanol (100 ml.) was hydrogenated for 6 hr. at 100°/100 atm. in hydrogen with Raney nickel (2 g.). The catalyst was removed and the alcoholic solution evaporated under reduced pressure, leaving a colourless amorphous *alcohol* (4·0 g.) (Found: C, 66·5, 66·6; H, 10·4, 10·0; active H, 1·1; *C*-Me, 13·0, 12·7. $C_{15}H_{26}O_4$ requires C, 66·7; H, 9·7; 3 active H, 1·1; 3*C*-Me, 16·7%). The product did not form a dinitrophenylhydrazone on treatment with Brady's reagent, and its infrared spectrum showed that a ketonic group was absent.

Acetylation of this tetrahydrotrichothecodiol gave an amorphous (?)triacetate [Found: C, 66·0, 65·7; H, 8·9, 8·9; Ac, 27·1. Calc. for $C_{21}H_{32}O_7$ (triacetate): C, 63·7; H, 8·1; Ac, 32·6. Calc. for $C_{19}H_{30}O_6$ (diacetate): C, 64·4; H, 8·5; Ac, 24·3%].

Dehydrogenation of Tetrahydrotrichothecodiol.—Tetrahydrotrichothecodiol (16 g.), mixed with 10% palladium–charcoal (16 g.), was placed in a 250 c.c. flask connected to a downward condenser. The receiver was cooled in ice, and the effluent gases were passed through 0·2N-barium hydroxide. The flask was heated (metal-bath) at a rate of about 2°/minute from 100° to 300° which was maintained for 4 hr. Distillation commenced at about 140°, became fairly rapid at 170°, and was slow at 200°. Distillates at atmospheric and 12 mm. pressure were collected. The residue in the flask was extracted successively with ether, acetone, and chloroform. The following fractions were collected: (*A*) Distillate at atmospheric pressure (7·414 g.) which consisted of (1) upper layer, greenish-yellow oil (3·615 g.) and (2) lower aqueous layer, colourless (3·715 g.). (*B*) Distillate at 12 mm., yellow oil (0·538 g.), containing a trace of water. (*C*) Ether-extract of flask residue, yellowish-brown oil (2·02 g.). (*D*) Combined acetone and chloroform extracts of flask residue, yellowish-brown oil (0·96 g.). (*E*) Washings from condenser and receiver (1·193 g.), containing an aqueous layer (0·1 g.). Total recovery was 12·125 g. (75·8%). Less than 0·1 mol. of carbon dioxide (0·19 g.) was recovered from the effluent gases.

Fraction (A2). The water content of the aqueous layer was determined by Fischer's method (Found: 78·6%, *i.e.*, 2·96 g., 2·754 mol.). The aqueous layer contained a mixture of ketones which were present in larger amounts and were isolated from the upper oily layer.

Fraction (A1). (i) The non-aqueous fraction (A1) (1·0 g.) was heated in 9 : 1 (v/v) ethanol–glacial acetic acid (10 ml.) with Girard T reagent (carbohydrazidotrimethylammonium chloride) (1·0 g.) for 1 hr., the ethanol removed at atmospheric pressure (distillate fraction *X*), and the non-volatile residue dissolved in water (25 ml.) and extracted with ether. The extract contained an oil (0·043 g.), b. p. 130—140°, which was found to be a mixture of a ketone and an oil. The aqueous solution after extraction with ether was acidified with N-hydrochloric acid, heated under reflux for 30 min., and extracted with ether. The residue from the extract (0·6515 g.) was separated into fractions (*a*) b. p. 34—40° (0·1075 g.), (*b*) b. p. 40—120° (0·123 g.), and (*c*) b. p. 120—134° (0·105 g.). Subfraction (*c*), with Brady's reagent, gave 2 : 3-*dimethyl*cyclo*pent-2-enone* 2 : 4-*dinitrophenylhydrazone* which crystallised from glacial acetic acid as red needles, m. p. 227—228° (corr.) (Found: C, 53·4; H, 4·7; N, 19·2; *C*-Me, 9·8. $C_{13}H_{14}O_4N_4$ requires C, 53·8; H, 4·8; N, 19·3; two *C*-Me, 10·3%). Subfraction (*b*) gave 2 : 3-*dimethyl*cyclo*pentanone* 2 : 4-*dinitrophenylhydrazone*, deep orange coloured plates (from ethanol), m. p. 156—157° (corr.) (Found: 53·4; H, 5·2; N, 19·5; *C*-Me, 10·3. $C_{13}H_{16}O_4N_4$ requires C, 53·4; H, 5·5; N, 19·2; 2*C*-Me, 10·3%).

The distillate fraction *X* was diluted with five volumes of water, and the resulting suspension extracted with ether. The residue from the ether-extract was distilled, giving a colourless mobile liquid (0·21 g.), b. p. 136—138° (Found: C, 90·2, 90·0; H, 9·7, 9·8. Calc. for C_8H_{10}: C, 90·6; H, 9·4%), n_D^{20} (Leitz–Jelley refractometer) 1·490 ± 0·001; *p*-xylene has b. p. 138·5° and n_D^{20} 1·494. The infrared spectrum of the hydrocarbon was identical with that of *p*-xylene over the range 2·5—13 μ. Nitration gave 2 : 3 : 5-trinitro-*p*-xylene, m. p. and mixed m. p. 138—139° (corr.) (Found: C, 40·2, 40·3; H, 3·3, 3·2; N, 17·1, 17·1. Calc. for $C_8H_7O_6N_3$: C, 39·8; H, 2·9; N, 17·4%).

(ii) A further quantity of fraction (A1) was treated with Girard T reagent as above, and the ketonic fraction separated. The latter (0·1 g.) was hydrogenated in the presence of 10% palladium–charcoal at atmospheric pressure. The product gave a 2 : 4-dinitrophenylhydrazone (by Brady's method) which crystallised from ethanol as orange plates, m. p. 156—157° (corr.) (Found: C, 53·4, 53·4; H, 5·6, 5·5; N, 19·2; *C*-Me, 10·3%). The hydrazone was identical with that of the *cyclo*pentanone isolated from fraction (*b*) as above. The *semicarbazone* crystallised from aqueous alcohol as rods, m. p. 206—207° (corr.) (Found: C, 56·5; H, 8·7; N, 25·2. $C_8H_{15}ON_3$ requires C, 56·8; H, 8·9; N, 24·8%). None of the m. p.s of the semicarbazones of 2 : 3-, 2 : 4-, and 2 : 5-dimethyl*cyclo*pentanones quoted in the literature corresponded to that of the semicarbazone of the unknown saturated ketone. Authentic 2 : 3-dimethyl*cyclo*pentanone was prepared by the method of Staudinger and Ruzicka,[22] and its semicarbazone had m. p. 206—207° (corr.) alone or mixed with the above semicarbazone (Dutta [23] records m. p. 179—180°). Authentic 2 : 3-dimethyl*cyclo*pentanone 2 : 4-dinitrophenylhydrazone melted at 156—157° (corr.) and the m. p. was undepressed on admixture with the above hydrazone. The infrared spectrum of the saturated ketone was identical with that of authentic 2 : 3-dimethyl*cyclo*pentanone.

(iii) *Identification of the unsaturated ketone with* 2 : 3-*dimethyl*cyclo*pent-2-enone.* 2 : 3-Dimethyl*cyclo*pent-2-enone was prepared by the method of Frank *et al.*[11] Its semicarbazone, m. p. 248—249° (decomp.), agreed satisfactorily in its properties with that of Frank *et al.* (m. p. 247—250°, decomp.). The m. p. of the 2 : 4-dinitrophenylhydrazone (m. p. 227—228°) was undepressed on admixture with the dinitrophenylhydrazone of the above unsaturated ketone (m. p. 227—228°). The ultraviolet absorption spectrum of 2 : 3-dimethyl*cyclo*pent-2-enone had maximum at 2335 Å (2290 Å for the above unsaturated ketone, which may have contained a trace of *p*-xylene).

Fractions (C) *and* (D). Fractions (*C*) and (*D*) were combined and steam-distilled. The volatile component was separated into fractions (i) b. p. 70—120°/10 mm. and (ii) b. p. 120—160°/10 mm. Fraction (i) was separated into fractions (i*a*) b. p. 200—220° (17% of steam-volatile oil) and (i*b*) b. p. 220—270°. Fraction (i*a*) contained a small quantity of 2 : 3-dimethyl*cyclo*pent-2-enone (isolated as 2 : 4-dinitrophenylhydrazone), and a hydroxylic compound which was difficultly soluble in sodium hydroxide solution and gave no colour reaction with ferric chloride and formed a 3 : 5-dinitrobenzoate, m. p. 131—134° (corr.) (Found: C, 57·7, 57·7; H, 3·9, 4·1; N, 8·4, 8·2; *C*-Me, 5·9. Calc. for $C_{15}H_{18}O_6N_2$: C, 57·0; H, 3·8; N, 8·9; 2*C*-Me, 9·5%). A mixed m. p. with authentic *p*-xylyl 3 : 5-dinitrobenzoate (m. p. 137°) was at 134—136°. The phenylurethane, m. p. 158—162° (corr.), did not depress the m. p. of authentic *p*-xylyl phenylurethane (m. p. 164°).

The carbonyl group in fraction (ii) (Found: C, 81·6; H, 9·7%) was reduced with lithium aluminium hydride, and the product dehydrogenated with an equal weight of 10% palladium–charcoal at 300° for 7 hr. Extraction of the product with ether gave a straw-coloured oil, b. p. 220—260°, in 40% yield (Found: C, 84·8; H, 9·8%), n_D^{16} 1·5174. The product had properties similar to those of the steam-volatile oil obtained by reduction of dihydrotrichothecolone with phosphorus and hydriodic acid.

Pyrolysis of Tetrahydrotrichothecodiol.—This diol (4·0 g.) and activated charcoal (4 g.) (undried) were heated at 300° for 2 hr. The distillate consisted of an oil (0·4 g.) and an aqueous layer (1·64 g.) containing 78·7% of water. The residue was extracted with solvents, giving a viscous oil (1·8 g.). The aqueous layer (1·64 g.) gave a 2 : 4-dinitrophenylhydrazone as red needles (from acetic acid), m. p. 225—226° (corr.) (0·04 g.), undepressed on admixture with 2 : 3-dimethyl*cyclo*pent-2-enone 2 : 4-dinitrophenylhydrazone (m. p. 227—228°). The infrared spectrum of the oil (0·4 g.) indicated the presence of *p*-xylene, together with a ketone.

High-pressure Hydrogenation of Trichothecolone Glycol (IV) *and Dehydrogenation of the Product.*—Trichothecolone glycol (5·5 g.) was hydrogenated at 100°/100 atm. in hydrogen for 6 hr. in the presence of Raney nickel. The amorphous product contained no ketonic group. The alcohol (5·6 g.) was dehydrogenated with 10% palladium–charcoal (6 g.) as described above. The distillate (2·866 g.) consisted of an oil (0·633 g.) and an aqueous layer (2·077 g.), containing 86·2% of water (5·05 mols.). The oil was fractionated with Girard T reagent, and *p*-xylene (0·27 g.) and a mixture of saturated and unsaturated ketones were isolated. Hydrogenation of the ketonic mixture gave 2 : 3-dimethyl*cyclo*pentanone.

[22] Staudinger and Ruzicka, *Helv. Chim. Acta*, 1924, **7**, 245.
[23] Dutta, *Science and Culture*, 1945, **10**, 355.

XUM

High-pressure Hydrogenation of Compound (VII) *and Dehydrogenation of the Product.*—Compound (VII) (4·6 g.) was hydrogenated at 100°/100 atm.; the product was a colourless, amorphous solid free from carbonyl groups. Dehydrogenation was carried out in the usual manner. The distillate (2·53 g.) consisted of a lower layer (1·49 g.), containing water (1·257 g.) (4 mols.) and an oil. *p*-Xylene and 2 : 3-dimethyl*cyclo*pent-2-enone were identified as components of the oil.

Dehydrogenation of the Saturated Acid (XX).—Acid (XX) (8·0 g.) was heated with 10% palladium–charcoal (8 g.). Distillation began at 250° and was very slow; the temperature was slowly raised to 340° and kept thereat for 4 hr. The distillate consisted of a lower layer (1·326 g.) containing water (1·127 g., 2·2 mols.), and a colourless upper layer (0·652 g.). Extraction of the residue in the distillation flask gave a yellow oil (1·6 g.), from which *p*-xylenol (0·8 g.) was isolated. The upper ketonic layer of distillate (0·2 g.) was hydrogenated at atmospheric pressure over palladium–charcoal. The product on distillation gave a colourless liquid (0·13 g.), b. p. 140°, from which a 2 : 4-dinitrophenylhydrazone, m. p. 161—162° (corr.), was obtained as golden needles from ethanol. The m. p. of the hydrazone was undepressed on admixture with authentic 2-methyl*cyclo*pentanone 2 : 4-dinitrophenylhydrazone (m. p. 160—161°) (Found: C, 52·8; H, 5·5; N, 19·3; *C*-Me, 7·6, 7·3. Calc. for $C_{12}H_{14}O_4N_4$: C, 51·8; H, 5·0; N, 20·1; *C*-Me, 5·4%). The *cyclo*pentanone also gave a semicarbazone, m. p. 180—181° (corr.), undepressed on admixture with authentic 2-methyl*cyclo*pentanone semicarbazone (m. p. 179—180°) (Found: C, 54·5; H, 8·6. Calc. for $C_{17}H_{13}ON_3$: C, 54·2; H, 8·4%). A mixed m. p. with 3-methyl*cyclo*pentanone semicarbazone (m. p. 180—181°) was 169°. The infrared spectrum of the ketone was identical with that of 2-methyl*cyclo*pentanone and differed from those of 3-methyl*cyclo*pentanone and the dimethyl*cyclo*pentanones described above. The spectrum of the dehydrogenation products showed no trace of an aromatic hydrocarbon.

Dehydrogenation of the Saturated Acid (XI).—Acid (XI) (10 g.) and 10% palladium–charcoal (10 g.) were heated as described above. Liberation of volatile products was not apparent until the bath-temperature reached 300° and distillation did not take place at a satisfactory rate until the temperature was raised to 370°. This temperature was maintained for 3 hr. The residue was extracted with ether, chloroform, and acetone. The distillate consisted of an oil (0·38 g.) and a lower layer (1·418 g.) containing water (1·316 g., 2·05 mols.). Hydrogenation of the oil (0·3 g.) at atmospheric pressure and distillation of the product gave a colourless liquid (0·15 g.), b. p. 140—150°; the latter gave a 2 : 4-dinitrophenylhydrazone which crystallised from ethanol in orange-yellow plates, m. p. 149—154° (corr.). Repeated recrystallisation, washing with hot light petroleum or chromatography on activated alumina, all failed to raise the m. p. of the hydrazone (Found: C, 52·4, 52·4; H, 5·0, 5·2; N, 20·1. Calc. for $C_{12}H_{14}O_4N_4$: C, 51·8; H, 5·0; N, 20·1%). A mixed m. p. with authentic 2-methyl*cyclo*pentanone 2 : 4-dinitrophenylhydrazone (m. p. 160—161°) was 155—158°. A mixed m. p. with 2 : 3-dimethyl*cyclo*pentanone 2 : 4-dinitrophenylhydrazone was 144—146°. Similarly, the semicarbazone, m. p. 169—172° (corr.) (from water), was not obtained pure. A mixed m. p. with authentic 2-methyl*cyclo*pentanone semicarbazone (m. p. 179—180°) was 171—176°, and with authentic 3-methyl*cyclo*pentanone semicarbazone (m. p. 183—185°) was 168—170°. The infrared spectrum of the unknown ketone showed bands characteristic of both 2- and 3-methyl*cyclo*pentanone, and it was concluded that a mixture of the two ketones had been obtained in which 2-methyl*cyclo*pentanone predominated. *p*-Xylenol (0·16 g.) was isolated from extracts of the still residue.

Alkaline Breakdown of Trichothecodione, etc.—(a) p-*Xyloquinone from trichothecodione.* When trichothecodione (0·15 g.) and 10% sodium hydroxide solution (15 ml.) were boiled under reflux, the solution darkened rapidly. After 5 min. the solution was cooled and extracted with chloroform. The extract (0·03 g.) on sublimation at 60°/20 mm. gave lemon-yellow crystals, which sintered at 110° and melted at 120—121° (Found: C, 69·9; H, 5·7. Calc. for $C_8H_8O_2$: C, 70·6; H, 5·9%) (mixed m. p. with *p*-xyloquinone undepressed), $\lambda_{max.}$ (in hexane) 2490 and 2560 Å (ε 21,400 and 19,000 respectively). For *p*-xyloquinone in hexane, Braude [21] gives maxima at 2500 and 2560 Å (ε 22,200 and 21,000 respectively). Comparison of the infrared spectrum of the sample with that of authentic *p*-xyloquinone showed them to be identical.

(b) p-*Xyloquinol from trichothecodione.* Trichothecodione (0·5 g.) and 10% sodium hydroxide solution (15 ml.) were boiled for 2 min. *p*-Xyloquinol (0·051 g.) was isolated from the products after acidification; it had m. p. and mixed m. p. 208—209° (Found: C, 69·6; H, 7·4. Calc. for $C_8H_{10}O_2$: C, 69·6; H, 7·25%).

[21] Braude, *J.*, 1945, 490.

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(c) *Acid* (XX). Acid (XX) (approx. 1 g.) was boiled in N-sodium hydroxide until a brown colour developed. Extraction of the alkaline solution with ether gave colourless plates (0·03 g.), m. p. 82—84°. This *substance* sublimed readily *in vacuo* at 100° (Found: C, 68·1; H, 8·6. $C_8H_{12}O_2$ requires C, 68·5; H, 8·6%).

Further C_{15} *and* C_{14} *Oxidation Products of Trichothecolone Derivatives.*—(i) *Compound* (VII). (*a*) Trichothecolone glycol (0·9 g.) was dissolved in 5% aqueous chromic acid solution (20 ml.); after a short time a *ketone* (0·323 g.) separated. After recrystallisation from methanol it melted at 228—229° [Found: C, 68·6, 68·3; H, 6·7, 6·9; *C*-Me, 14·5; active H, 0·51%; *M* (by *X*-ray method), 259. $C_{15}H_{18}O_4$ requires C, 68·7; H, 6·9; 2*C*-Me, 11·5; 3*C*-Me, 17·2; 1 active H, 0·38%; *M*, 262].

(*b*) Trichothecolone glycol (1·0 g.) and periodic acid (0·7 g.) in water (40 ml.) were kept at room temperature in the dark for 8 days. Fern-like crystals separated, and an estimation of the excess of periodic acid showed that it had been almost completely consumed. The product (0·09 g.) crystallised from ethanol in colourless elongated prisms, m. p. 236—237° (corr.) (Found: C, 68·55; H, 6·5; active H, 0·45; *C*-Me, 15·0%) (the compound sublimed unaltered at 200°/0·1 mm.), identical (mixed m. p. and infrared spectra) with that obtained by method (*a*).

The 2 : 4-*dinitrophenylhydrazone* of the ketone (VII) crystallised from acetic acid in orange prisms, m. p. 302° (decomp.) (Found: C, 56·7; H, 4·8; N, 12·4. $C_{21}H_{22}O_7N_4$ requires C, 57·0; H, 5·0; N, 12·7%). The ketone (0·1 g.) with acetic anhydride gave a *monoacetate* (0·1 g.), m. p. 133°, prisms (from methanol) (Found: C, 67·4, 67·2; H, 6·5, 6·7; Ac, 18·3. $C_{17}H_{20}O_5$ requires C, 67·0; H, 6·6; 1Ac, 14·2%), $\lambda_{max.}$ (in methanol) 2290 Å (ε 12,750).

Compound (VII) (0·21 g.) absorbed hydrogen (50 ml.) in 5 min. when shaken in the presence of palladium–charcoal. The product was a *ketone* (VIII) (0·205 g.), m. p. 165—166°, needles (from methanol) (Found: C, 67·8, 67·4; H, 8·2, 8·3. $C_{15}H_{22}O_4$ requires C, 67·7; H, 8·3%), whose yellow 2 : 4-*dinitrophenylhydrazone* (from methanol) had m. p. 266° (decomp.) (Found: C, 56·4; H, 5·5; N, 12·6. $C_{21}H_{26}O_7N_4$ requires C, 56·5; H, 5·8; N, 12·6%).

(ii) *Compound* (IX). Dihydrotrichothecolone glycol (1·0 g.) with aqueous chromic acid, as described above, gave a *ketone* (IX) (0·5 g.), m. p. 185—186°, needles (from benzene) (Found: C, 68·5, 68·2; H, 7·4, 7·6. $C_{15}H_{20}O_4$ requires C, 68·2; H, 7·5%), whose orange 2 : 4-*dinitrophenylhydrazone*, crystallised from acetic acid, had m. p. 264—265° (Found: C, 55·7, 55·4; H, 5·6, 5·2; N, 12·1. $C_{21}H_{24}O_7N_4$ requires C, 57·7; H, 5·4; N, 12·6%).

(iii) *Acid* (XI). Oxidation of compound (VIII) (0·15 g.) in glacial acetic acid (1 ml.) with 5% chromic acid in acetic acid (5 ml.) at 34° yielded *acid* (XI) (0·04 g.), m. p. 184—185° (decomp.), as prisms from hot water (Found: C, 64·2; H, 7·1%; equiv., 291. $C_{15}H_{20}O_5$ requires C, 64·3; H, 7·1%; equiv., 280). The infrared absorption spectrum showed absorption between 2500 and 3200 cm.$^{-1}$, confirming the presence of a carboxyl group, and bands in the carbonyl region at 1685, 1722 (weak), and 1750 cm.$^{-1}$. This acid was also prepared by hydrogenation of acid (X) and of acid (XII) (described below).

(iv) *Acid* (X). Compound (VII) (0·45 g.) was oxidised with chromic acid in acetic acid at 33°. The product, *acid* (X) (0·146 g.), m. p. 187—188° (decomp.), crystallised from hot water in needles (Found: C, 61·2, 61·3; H, 6·0, 5·7. $C_{15}H_{16}O_5,H_2O$ requires C, 61·2; H, 6·1%). A sample after 2·5 hours' drying at 120° became opaque (Found: C, 64·7; H, 5·7. $C_{15}H_{16}O_5$ requires C, 65·2; H, 5·8%), $\lambda_{max.}$ (in methanol) 2270 Å (ε 12,500), $\nu_{max.}$ 3530 (OH-hydrate), 2700—2800 (CO_2H), and CO bands at 1720 and 1675 cm.$^{-1}$. The acid gave no colour with ferric chloride.

The preceding hydrate (0·18 g.) in methanol was shaken with hydrogen in the presence of palladium–charcoal, 40 ml. of hydrogen being absorbed at 21° during 5 min. ($2H_2$ = 31 ml. at N.T.P.). The product, acid (XI) (0·14 g.) crystallised from hot water as needles, m. p. 182—183° (decomp.) (Found: C, 63·9; H, 6·9%). A mixed m. p. with acid (XI) obtained by oxidation of compound (VIII) was undepressed.

(v) *Acid* (XII). On oxidation with chromic acid in acetic acid, compound (IX) (0·2 g.) gave *acid* (XII) as *hydrate* (0·093 g.), which crystallised from hot water as prisms, m. p. 205—206° (decomp.) (Found: C, 60·4, 60·7; H, 6·4, 6·4. $C_{15}H_{18}O_5,H_2O$ requires C, 60·8; H, 6·7%. Found, after drying at 100°: C, 64·6; H, 6·7. $C_{15}H_{18}O_5$ requires C, 64·8; H, 6·5%). The acid gave no colour with ferric chloride.

Acid (XII) (0·1 g.) in methanol absorbed hydrogen (13 ml.) in 5 min. in the presence of palladium–charcoal at 17°. On recrystallisation from water the product formed prisms of acid

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(XI) (0·06 g.), m. p. 184—185° (decomp.) (Found: C, 64·0, 64·0; H, 7·4, 7·0%). A mixed m. p. with acid (XI) prepared by oxidation of (VIII) was undepressed. The acid gave no colour with ferric chloride.

Ketone (XIII): *Decarboxylation of Acid* (X).—Acid (X) (0·223 g.), when heated at 210° for 3 min., melted and effervesced vigorously, losing carbon dioxide. The melt solidified on cooling, and after trituration with ether it was obtained as a colourless insoluble powder (0·138 g.). *Ketone* (XIII) sublimed at 150—160°/20 mm. as plates, m. p. 132—133° (Found: 72·2, 71·8; H, 7·0, 6·6. $C_{14}H_{16}O_3$ requires C, 72·4; H, 6·9%), $\lambda_{max.}$ (in methanol) 2230 Å (ε 11,500). The infrared absorption spectrum showed the absence of bands due to carboxyl groups, and the presence of two carbonyl bands at 1720 and 1680 cm.$^{-1}$. Ketone (XIII) formed a 2 : 4-dinitrophenylhydrazone which was obtained as orange needles, m. p. 255—256° (decomp.).

Ketone (XIV): *Decarboxylation of Acid* (XI).—On decarboxylation, acid (XI) (0·5 g.) gave *ketone* (XIV) (0·177 g.) as needles, m. p. 110—112° [from light petroleum (b. p. 60—80°)] (Found: C, 70·9; H, 8·9. $C_{14}H_{20}O_3$ requires C, 71·2; H, 8·5%), $\nu_{max.}$ (>CO) 1710 and 1740 cm.$^{-1}$. This ketone (XIV) (0·1 g.) gave prisms (from chloroform) of a *bis-semicarbazone* (0·07 g.), m. p. 230° (decomp.), which gave a weakly positive Beilstein halogen test [Found: C, 47·8, 48·7; H, 6·8, 7·0; N, 19·5, 19·7. $(C_{16}H_{26}O_3N_6)_2,CHCl_3$ requires C, 48·3; H, 6·5; N, 20·5%], and a deep orange *bis*-2 : 4-*dinitrophenylhydrazone*, m. p. 250—252° (decomp.) (Found: C, 53·8, 54·2; H, 5·2, 5·4; N, 17·2, 16·8. $C_{36}H_{38}O_9N_8$ requires C, 52·4; H, 4·7; N, 18·8. Calc. for $C_{20}H_{24}O_6N_4$: C, 57·7; H, 5·8; N, 13·5%).

Ketone (XV): *Decarboxylation of Acid* (XII).—Acid (XII) (0·07 g.) was decarboxylated by heating at 220°. The product (0·026 g.) was *ketone* (XV), which was purified by sublimation at 140—150°/0·6 mm. and obtained as needles, m. p. 158—160° (Found: C, 71·9, 72·0; H, 7·7, 7·8. $C_{14}H_{18}O_3$ requires C, 71·8; H, 7·7%).

neo*Trichothecodione*.—(*a*) Trichothecodione (0·25 g.) was heated on a water-bath for 1 hr. with concentrated ammonia solution (7 ml.; *d* 0·880). The dark brown solution was cooled and extracted with chloroform. Evaporation of the chloroform left a dark solid (0·19 g.) which was dissolved in benzene (10 ml.) and decolorised by boiling it with charcoal. neo-*Trichothecodione* (XVI) was precipitated by addition of light petroleum and obtained as irregular cream-coloured crystals, m. p. 165—166° (corr.), which were nitrogen-free [Found: C, 68·4, 68·4; H, 6·6, 6·8%; *M* (Rast), 257. $C_{15}H_{18}O_4$ requires C, 68·7; H, 6·9%; *M*, 262].

(*b*) Trichothecodione (1·0 g.) was dissolved in methanol (35 ml.) at 50°, and anhydrous sodium carbonate (1·0 g.) in water (35 ml.) added. The solution was heated to 60° for 10 min., and the methanol then removed *in vacuo*. Addition of water (20 ml.) to the residual solution caused *neo*trichothecodione to separate as colourless prisms (0·971 g.), m. p. 168—169° (corr.).

(*c*) Trichothecodione (0·130 g.) was dissolved in boiling methanol (6 ml.), and 0·1N-sodium hydroxide (5 ml., one equiv.) added. The solution was heated under reflux for 3 min., then cooled, water (5 ml.) was added, and the whole extracted with chloroform. Removal of the solvent gave *neo*trichothecodione (0·08 g.), m. p. 162—163°. Estimation of ethylenic double bonds by hydrogenation showed that two were present.

neo*Trichothecodione* 2 : 4-*dinitrophenylhydrazone* crystallised from ethanol in yellow needles, m. p. 268° (corr.) (Found: C, 57·2, 57·4; H, 5·0, 5·2; N, 12·5, 12·6. $C_{21}H_{22}O_7N_4$ requires C, 57·0; H, 5·0; N, 12·7%).

neo*Dihydrotrichothecodione*.—Similar treatment of dihydrotrichothecodione (1·0 g.) with sodium carbonate yielded the neo*dihydro-dione* (0·96 g.), which recrystallised from benzene–light petroleum as colourless needles, m. p. 136—136·5° (corr.) (Found: C, 68·5, 68·4; H, 7·5, 7·5. $C_{15}H_{20}O_4$ requires C, 68·2; H, 7·6%), $\lambda_{max.}$ (in methanol), 2150 Å (ε 7280). It gave an orange *mono*-2 : 4-*dinitrophenylhydrazone* (from ethanol), m. p. 245° (Found: C, 56·6, 56·5; H, 5·4, 5·4; N, 12·7, 12·2. $C_{21}H_{24}O_7N_4$ requires C, 56·8; H, 5·4; N, 12·6%).

Reaction of Dihydrotrichothecodione with Dilute Hydrochloric Acid.—Dihydrotrichothecodione (0·1 g.) in N-hydrochloric acid (3 ml.) was boiled for 30 min. Extraction with chloroform gave a soft colourless product (0·1 g.) which was precipitated from benzene solution by addition of light petroleum as an amorphous mass which slowly crystallised on long standing, giving conglomerates of crystals, m. p. 108—110° (corr.). A mixed m. p. with *neo*dihydrotrichothecodione (m. p. 135°) was 120—121°.

Oxidation of neo*Trichothecodione and Trichothecolone Chlorohydrin: Acid* (XVIII).—(*a*) On oxidation with chromic acid in acetic acid by the method described above, *neo*trichothecodione (0·5 g.) gave *acid* (XVIII) as colourless prisms (from benzene–light petroleum) (0·35 g.), m. p.

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173—174° (corr.) (Found: C, 64·8, 64·7; H, 5·9, 5·7%; equiv., 273. $C_{15}H_{16}O_5$ requires C, 65·2; H, 5·8%; equiv., 276). The acid was not decarboxylated on melting. If the acid was isolated by extraction into sodium hydrogen carbonate solution and precipitated by dilute sulphuric acid, the product was obtained as a hydrate, m. p. 115—116° with previous sintering, undepressed on admixture with acid (XVIII) prepared by oxidation of trichothecolone chlorohydrin (described below). *X*-Ray photographs confirmed that these two acids were identical. The hydrated acid crystallised from hot water in colourless needles, which sintered about 105° and melted 115—116°. A sample dried at 100° had m. p. 173—174°, unchanged after recrystallisation from benzene.

(*b*) In a similar way, trichothecolone chlorohydrin (0·2 g.) gave acid (XVIII) as needles (from aqueous methanol) (0·197 g.), m. p. 115—116° (Found: C, 60·9, 60·9; H, 6·4, 5·9. $C_{15}H_{16}O_5,H_2O$ requires C, 61·2; H, 6·1%), $\lambda_{max.}$ (in methanol) 2220 Å (ε 12,220), $\nu_{max.}$ 3480 s (hydrate), ~2500 (CO_2H) and 1740, 1708, and 1670 cm.$^{-1}$ (>CO, last three).

Acid (XIX).—(a) *By oxidation of dihydrotrichothecolone chlorohydrin.* The corresponding oxidation product from dihydrotrichothecolone chlorohydrin (0·3 g.) was large colourless plates of an unstable *hydrate*, m. p. 53—54° (Found: C, 59·7; H, 6·7. $C_{15}H_{18}O_5,H_2O$ requires C, 60·8; H, 6·8%). When kept at room temperature or dried at 42°, the crystals lost water and became opaque, giving anhydrous *acid* (XIX) which crystallised from benzene–light petroleum (b. p. 40—60°) as needles, m. p. 163—164°. The acid was not decarboxylated on melting, but on cooling the melt resolidified and then remelted at 198° (Found: C, 65·0, 64·5; H, 6·4, 6·5. $C_{15}H_{18}O_5$ requires C, 64·8; H, 6·5%), $\lambda_{max.}$ (in methanol), 2170 Å (ε 7670).

(b) *By oxidation of* neo*dihydrotrichothecodione.* The same acid (0·092 g.) was obtained by oxidation of *neo*dihydrotrichothecodione (0·2 g.) as needles (from benzene–light petroleum), m. p. 161·5—162·5° (corr.), which resolidified and remelted at 208° (corr.) (Found: C, 64·8; H, 6·4%).

Acid (XIX) was recovered unchanged after 2 minutes' heating at 210—220° and distilled at 200°/0·05 mm.

The anhydrous acid, prepared by oxidation of dihydrotrichothecolone chlorohydrin, gave the 2 : 4-*dinitrophenylhydrazone*, orange-yellow needles (from methanol), m. p. 254—255° (decomp.) (Found: N, 12·2. $C_{21}H_{22}O_8N_4$ requires N, 12·2%). Mixed m. p.s of the hydrazones (m. p. 251—252°) obtained by oxidation of the hydroxy-chloro-acid (XXI; R = H) from dihydrotrichothecodione chlorohydrin and from dihydrotrichothecolone chlorohydrin were undepressed.

Dihydrotrichothecodione chlorohydrin (0·2 g.) was oxidised with chromic acid in acetic acid, and the product treated with Brady's reagent. The preceding 2 : 4-dinitrophenylhydrazone (0·065 g.), orange prisms (from methanol), m. p. 251—252° (decomp.) (Found: C, 54·8; H, 4·9; Cl, 0. $C_{21}H_{22}O_8N_4$ requires C, 55·0; H, 4·8%), was again obtained.

Similarly the hydroxy-chloro-acid (XXI; R = H) (0·086 g.), prepared by oxidation of tetrahydrotrichothecin chlorohydrin and hydrolysis of the product, was oxidised with aqueous chromic acid. The crude product (0·028 g.) gave once more the same 2 : 4-dinitrophenylhydrazone, orange prisms (from methanol), m. p. 251—252° (decomp.) (0·012 g.).

X-Ray powder photographs of the hydrazones prepared by the three methods, described above, confirmed their identity.

Acid (XX).—(a) *By hydrogenation of acid* (XVIII). Acid (XVIII) (0·177 g.) (prepared from *neo*trichothecodione) absorbed hydrogen (28 ml.) at 22° in the presence of palladium–charcoal in 5 min. The product crystallised from benzene, giving colourless prisms of acid (XX), m. p. 187—188° {mixed m. p. 183—184° with (XX) (prepared from dihydrotrichothecolone chlorohydrin) (m. p. 183—184°). Mixed m. p. 187—188° with (XX) [prepared by oxidation of (XVII)], m. p. 187—189°}. The infrared absorption spectrum showed carbonyl bands at 1700 and 1730 cm.$^{-1}$. Acid (XVIII) (0·193 g.) (prepared from trichothecolone chlorohydrin) absorbed hydrogen (26 ml.) at 21° in 5 min. in the presence of palladium–charcoal, giving *acid* (XX), prisms (from benzene), m. p. 185—186° (0·072 g.) (Found: C, 64·1, 64·2; H, 6·8, 6·9. $C_{15}H_{20}O_5$ requires C, 64·3; H, 7·1%). The acid did not decompose on melting and gave no colour with ferric chloride.

(b) *By hydrogenation of acid* (XIX). Similarly, acid (XIX) (0·2 g.) (prepared from *neo*-dihydrotrichothecodione) absorbed hydrogen (23 ml.) in 2 min. at 21° in the presence of palladium–charcoal. The product crystallised from benzene in prisms m. p. 187—188°; the mixed m. p. with acid (XX) [prepared from (XVIII)], m. p. 187—188°, was undepressed.

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(c) *By oxidation of compound* (XVII). Compound (XVII) (0·15 g.) was oxidised with chromic acid in acetic acid, giving acid (XX) (0·072 g.) as prisms, m. p. 187—189° (from benzene) (Found: C, 63·9, 64·1; H, 7·0, 7·5%), mixed m. p. 185—187° with (XX) [prepared by hydrogenation of (XVIII) from the trichothecolone chlorohydrin series], m. p. 185—186°.

Compound (XVII).—(a) *By hydrogenation of* neo*trichothecodione*. *neo*Trichothecodione (0·2 g.) in methanol absorbed hydrogen (33 ml.) at 21° in 5 min. in the presence of palladium–charcoal, *i.e.*, 31 ml. at N.T.P. ($2H_2$ = 34 ml. at N.T.P.). *Ketone* (XVII) crystallised from methanol and melted at 192—193° (Found: C, 67·3, 67·5; H, 8·5, 8·4. $C_{15}H_{22}O_4$ requires C, 67·7; H, 8·3%).

(b) *By hydrogenation of* neo*dihydrotrichothecodione*. Similarly, *neo*dihydrotrichothecodione (0·2 g.) absorbed hydrogen (14 ml.) in 5 min. at 23° (*i.e.*, 13 ml. at N.T.P.; H_2 = 17 ml.). The product (XVII) crystallised in prisms, m. p. 192—193°, undepressed on admixture with the product of hydrogenation of *neo*trichothecodione. The infrared spectrum showed a strong hydroxyl band, and carbonyl bands at 1722 and 1690 cm.$^{-1}$.

Methyl Ester of Acid (XX).—The acid (0·5 g.) was esterified with diazomethane. The *ester* crystallised from light petroleum (b. p. 60—80°) as prisms, m. p. 101—102° (Found: C, 65·0, 65·1; H, 7·2, 7·6. $C_{16}H_{22}O_5$ requires C, 65·3; H, 7·5%). The infrared spectrum showed a broad band of carbonyl absorption (which may be double) at about 1725 cm.$^{-1}$.

Tests for Oxide Ring.—Group 1. The compounds of this group gave a strong positive reaction with the reagent at 60—70° in, usually, 10—15 min. The red colour due to the indicator rapidly increased in intensity with the time of heating. The times recorded are approximate. Compound (VII) gave a yellow solution in 30 min., and before hydroxyl ions were liberated. There was a marked difference between the behaviour of this compound and compounds of the *neo*trichothecodione series.

Compound	Time for colour to develop (min.)	Compound	Time for colour to develop (min.)
Trichothecolone	10	*neo*Trichothecodione	5
Dihydrotrichothecolone	15	*neo*Dihydrotrichothecodione	20
Trichothecodione	10	Compound (VII)	120
Dihydrotrichothecodione	10		

Group 2. The compounds of this group gave only weak pink colours, which did not increase in intensity, and in most cases faded. These weak colours were very slow to develop.

Compound	Time for colour to develop
Acetyltrichothecolone	20 min. (fades)
Butyryltrichothecolone	60 min. (fades after 2 hr.)
*iso*Trichothecolone	1—2 hr.
Trichothecolone glycol	2 hr. (extremely faint)
Trichothecolone chlorohydrin	1 hr. (fades after 2 hr.)

Group 3. The compounds of this group gave no colours even after many hours' heating.

Compound	Time heated (hr.)	Compound	Time heated (hr.)
Tricothecin	5	Trichothecin chlorohydrin	2
Trichothecin glycol	2	Crotonyltrichothecolone	3

Comparative experiments were carried out under similar conditions with oxide rings of various sizes, with the following results:

Three-membered oxide rings:	
Propylene oxide	Pink immediately in the cold.
Phorone dioxide	Pink after 3 min. in the cold, or immediately at 50°.
Et *cyclo*hexane*spiro*-2-oxiran-3-carboxylate	No colour after 3 hr. at 70°.
Glycidyl acetate	Pink colour immediately in the cold.
Four-membered oxide rings:	
3 : 3-Dimethyloxetan	No colour after 3 hr. at 70°.
3 : 3-Diacetoxymethyloxetan	No colour after 3 hr. at 70°.
Trimethylene oxide	Pink after 2 min. at 70°; pale pink after 20 min. in the cold.
Five-membered oxide rings:	
Tetrahydrofuran	Extremely weak colour after 40 min. at 70°; fades after 2 hr.
Six-membered oxide rings:	
Tetrahydropyran	No colour after 3 hr. at 70°.
Dihydropyran	Extremely weak colour after 3 hr. at 70°.

Heat of Reaction of Trichothecolone with Hydrochloric Acid (*by* T. COTTRELL, R. A. HAMILTON, and R. P. TAUBINGER).—The reaction between trichothecolone and hydrochloric acid involves the breaking of an ether-type C–O link: in terms of bonds the reaction is: C–O + H–Cl ⟶ C–Cl + H–O. Consideration of bond-energy terms suggests that this reaction will be about thermally neutral, and it therefore seems reasonable to believe that any heat evolved in the reaction of trichothecolone with hydrochloric acid will be due to ring rupture and thus will give an indication of ring strain. In case the bond reaction itself might not be exactly neutral, the reaction of epichlorohydrin with hydrochloric acid was examined for comparison. Measurements were carried out by using a conventional Dewar vessel calorimeter, the heat capacity of the system being determined by measuring the temperature rise on dilution of 37% hydrochloric acid. The experimental accuracy was probably about ±5%. Three measurements were made for epichlorohydrin, giving $-\Delta H$ for the reaction:

$$\text{epichlorohydrin } (l) + \text{HCl (37\%, aq.)} \longrightarrow \text{Products} \quad . \quad . \quad . \quad . \quad (1)$$

as 27·8, 29·4, and 29·5 kcal. mole^{-1} respectively. Thus $-\Delta H$ (1) = 29 kcal. mole^{-1}. Initially two measurements of $-\Delta H$ for the reaction:

$$\text{Trichothecolone } (s) + \text{HCl (37\% aq.)} \longrightarrow \text{Products} \quad . \quad . \quad . \quad . \quad (2)$$

gave 26·5 and 28·9 kcal. mole^{-1}. Two further measurements on another specimen of trichothecolone gave 23·2 and 22·9 kcal. mole^{-1}. There appears to have been a difference between the two samples, so that the value of $-\Delta H$ (2), 25 kcal. mole^{-1}, is subject to an unknown uncertainty. These results are in good agreement with the expected range of values, considering that unknown heats of solution and fusion are involved in the measured quantities.

Miscellaneous Reactions of Trichothecolone and its Derivatives.—Reduction of dihydrotrichothecolone with phosphorus and hydriodic acid. Dihydrotrichothecolone (2·0 g.), red phosphorus (0·5 g.), and hydriodic acid (35 ml.; *d* 1·7) were heated under reflux for 42 hr. Within a short time an immiscible oil was refluxing in the condenser. The mixture was cooled, diluted with water, and extracted with ether. The extract was washed successively with 5% sodium hydroxide solution, sodium thiosulphate solution, and water, and the solvent was then removed. The residue was steam-distilled and the pale yellow oil in the distillate extracted with ether. Removal of the solvent left a mobile oil (0·3 g.) which sublimed at 100°/20 mm. and had a b. p. (Siwoloboff's method) between 230° and 240° (yield 0·135 g.). Most preparations contained a trace of halogen, but a sample distilled over sodium gave a liquid, n_D^{22} 1·5130, free from halogen (Found: C, 86·6; H, 10·9%). Another sample, $n_D^{21\cdot5}$ 1·5252, examined on a mass spectrograph, contained a fraction of molecular weight 206, this being the mass : charge ratio of the heaviest abundant ion present. The product showed no aromatic absorption bands in its infrared spectrum.

Reduction of trichothecin with Adams catalyst. Trichothecin (1·0 g.) in methanol absorbed hydrogen (200 ml.) at 21° during 30 min. in the presence of Adams catalyst ($3H_2$ = 202 ml.). The product, a viscous oil, was hydrolysed with 6% methanolic potassium hydroxide (40 ml.). Chloroform extraction gave a *compound* (0·868 g.) which crystallised from benzene in colourless prisms (0·212 g.), m. p. 138° (Found: C, 67·4, 67·2; H, 9·2, 9·0. $C_{15}H_{24}O_4$ requires C, 67·2; H, 9·0%). The infrared absorption spectrum showed no carbonyl groups, but two bands were present at the hydroxyl frequency.

Permanganate oxidations of trichothecolone derivatives. Acetic acid was isolated on alkaline permanganate oxidation of trichothecolone glycol; oxalic acid from the oxidation of *iso*trichothecolone and dihydro*iso*trichothecolone. Oxidation of dihydrotrichothecolone with acid permanganate gave a small yield of dihydrotrichothecodione.

X-*Ray Examination of Halogenated Derivatives* (*by* Dr. J. A. JARVIS).—The following crystalline derivatives of trichothecin were submitted to *X*-ray examination:

(1) C_{19}-bromo acid. Orthorhombic: a = 9·0, b = 9·9, c = 22·1 Å. Space group $P2_12_12_1$, 4 molecules per cell.

(2) C_{19}-chloro-acid (XXI; R = Pr·CO); isomorphous with above.

(3) Trichothecin bromohydrin; monoclinic; a = 20·4, b = 6·1, c = 16·3 Å, β = 96°, space group $A2$, 4 molecules per cell.

(4) Trichothecin chlorohydrin; material recrystallised from aqueous alcohol or aqueous acetic acid was not isomorphous with the bromohydrin.

XUM

Zero-layer Weissenberg photographs have been taken of the isomorphous C_{19} acids about their *a* and *b* axes. Comparison of Patterson projections for the two compounds gave co-ordinates of halogen atoms. By using these co-ordinates it was possible to calculate values of $F_{Br} - F_{Cl}$ and hence the signs of many structure amplitudes. Study of the *a* and *b* axis projections of the C_{19} chloro-acid reduced the residual *R* to 22%. The 4-chloro-2-nitrophenylhydrazones of trichothecolone chloro- and bromo-hydrins were isomorphous and had the following cell dimensions: chloro-compound, *a* 20·56, *b* 7·09, *c* 7·90 Å, β 98·5°; bromo-compound, *a* 20·83, *b* 7·09, *c* 7·88 Å, β 98·5°.

iso*Trichothecolone*.—iso*Trichothecolone* was formed from trichothecolone in practically quantitative yields, or directly from trichothecin, by the action of hot aqueous or alcoholic sodium or barium hydroxides. Trichothecolone (2·5 g.)was completely isomerised after 30 min. in boiling N-sodium hydroxide (50 ml.) and ethanol (30 ml.). *iso*Trichothecolone crystallised in colourless needles [from benzene–light petroleum (1 : 1)], m. p. 184—185° (corr.), depressed to 154° on admixture with trichothecolone [m. p. 183—184° (corr.)] [Found: C, 68·0, 67·9; H, 7·6, 7·5; *C*-Me, 10·7; active H, 0·64%; *M* (Rast), 293, 279. $C_{15}H_{20}O_4$ requires C, 68·2; H, 7·6; 2*C*-Me, 11·4; 3*C*-Me, 17·0; 2 active H, 0·76%; *M*, 264]. *iso*Trichothecolone had $[\alpha]_D^{17·5}$ −38° (*c* 1 in ethanol), $\lambda_{max.}$ (in methanol), 2300 Å (ε 8050).

Its 2 : 4-*dinitrophenylhydrazone* crystallised from ethanol as deep orange needles, m. p. 252° (corr.) (Found: C, 55·8; H, 5·6; N, 12·5, 12·5. $C_{21}H_{24}O_7N_4$ requires C, 56·9; H, 5·4; N, 12·6%), and the *mono*-p-*nitrobenzoate* from *iso*trichothecolone (1·5 g.) separated from benzene–light petroleum as an amorphous solid (1·27 g.), m. p. 195—196° (corr.) (Found: C, 63·8, 63·6; H, 5·7, 5·5; N, 3·6, 3·7. $C_{22}H_{23}O_7N$ requires C, 63·9; H, 5·6; N, 3·4%).

Dihydroisotrichothecolone.—(*a*) *iso*Trichothecolone (0·2 g.) was hydrogenated in ethanol (25 ml.) at 1 atm. with 10% palladium–charcoal (0·2 g.). Absorption of hydrogen was complete in 2 min. (17·5 ml. at N.T.P.; $1H_2 = 17$ ml.). The crude product (0·206 g.) was extracted with benzene; the residue was crystalline *dihydroisotrichothecolone* (0·1 g.) which recrystallised from chloroform–light petroleum (1 : 4) as colourless rods, m. p. 199—201° (corr.) [Found: C, 66·8; H, 8·1%; *M* (Rast), 250. $C_{15}H_{22}O_4$ requires C, 67·7; H, 8·3%; *M*, 266], $[\alpha]_D^{20}$ −1·2° ± 0·5° (*c* 3·9 in acetic acid). Evaporation of the benzene extract gave a crystalline residue, m. p. 130—132° (corr.), undepressed on admixture with dihydro*iso*trichothecolone (m. p. 132°) obtained by the action of hot alkali on dihydrotrichothecolone or by hydrolysis of hydrogenated acetyl*iso*trichothecolone (Found: C, 67·3, 67·4; H, 8·2, 8·4%), $[\alpha]_D^{20}$ −114° (*c* 3·8 in acetic acid). The infrared spectra of the above specimens of dihydro*iso*trichothecolone were identical in their principal bands, but differed very slightly in detail in the 8—13 μ region.

(*b*) Dihydrotrichothecolone (0·25 g.) was heated with methanolic potassium hydroxide (12 ml.). The product (0·244 g.) crystallised from benzene–light petroleum (1 : 1) as a new form (prisms), m. p. 130—132° (corr.) (Found: C, 67·3, 67·4; H, 8·2, 8·4%).

Dihydro*iso*trichothecolone, m. p. 132°, was recovered unchanged after 2 hours' boiling in 0·1N-hydrochloric acid. The same 2 : 4-*dinitrophenylhydrazone* was prepared from both forms and crystallised as pale orange needles from ethanol and had m. p. 185—186° (Found: C, 55·3, 55·4; H, 6·2, 6·0; N, 11·5, 11·8. $C_{21}H_{26}O_7N_4$ requires C, 56·5; H, 5·8; N, 12·5%), $[\alpha]_D^{19·5}$ −347° (*c* 0·5 in acetic acid).

Dihydro*iso*trichothecolone, m. p. 199—201° (0·5 g.), was heated under reflux with N-sodium hydroxide (25 ml.) for 3 hr.; the product isolated by extraction with chloroform (0·46 g.) had m. p. 128—131°, undepressed on admixture with dihydro*iso*trichothecolone, m. p. 132°. It had $[\alpha]_D^{16·5}$ −113° (*c* 1·3 in ethanol).

Dihydro*iso*trichothecolone, m. p. 199—201° (0·4 g.), was dissolved in ethanol (25 ml.), and concentrated hydrochloric acid (5 ml.) added to bring the normality of the solution to 2N. The solution was kept at room temperature for 4 hr., then it had $[\alpha]_D^{19·5}$ −116° (*c* 1·3 in 2N-ethanolic hydrochloric acid), virtually identical with that of dihydro*iso*trichothecolone, m. p. 132°.

Monoacetylisotrichothecolone.—*iso*Trichothecolone was heated with acetic anhydride in pyridine for 30 min. The *acetate* crystallised from benzene–light petroleum (1 : 1) in colourless needles, m. p. 185—186° (corr.) (Found: C, 66·5; H, 7·3; Ac, 18·8, 18·3. $C_{17}H_{22}O_5$ requires C, 66·6; H, 7·2; 1Ac, 14·1%). It was also obtained by heating *iso*trichothecolone under reflux for 30 hr. with glacial acetic acid. It had infrared bands at 3400 (OH), 1650 (C:C), 1750 cm.$^{-1}$ (ester CO), but the band at 1667 cm.$^{-1}$, due to the original ketonic group, was absent.

Hydrogenation of Monoacetylisotrichothecolone.—The acetate was hydrogenated at 1 atm.

with 10% palladium–charcoal, with uptake of one mol. of hydrogen. *Acetyldihydroiso**trichothecolone*** crystallised from benzene–light petroleum (1 : 4) in colourless needles containing benzene of crystallisation, had m. p. 123—124° (corr.) (Found: C, 71·9; H, 8·0. $C_{17}H_{24}O_5,C_6H_6$ requires C, 71·6; H, 7·8%). Hydrolysis of the acetyl derivative with methanolic potassium hydroxide gave dihydro*iso*trichothecolone, m. p. 126—130°, undepressed on admixture with dihydro*iso*trichothecolone of m. p. 132° prepared by the action of hot alcoholic potassium hydroxide on dihydrotrichothecolone. Acetyldihydro*iso*trichothecolone was also prepared from either form of dihydro*iso*trichothecolone by acetic anhydride in pyridine. The product crystallised as small aggregates [from benzene–light petroleum (2 : 1)], m. p. 120—121°, undepressed on admixture with acetyldihydro*iso*trichothecolone (m. p. 123—124°) prepared by hydrogenation of acetyl*iso*trichothecolone.

*Diacetyliso**trichothecolone***.—*iso*Trichothecolone (1·0 g.) was heated under reflux for 4 hr. with acetic anhydride (5 ml.) and sodium acetate (1 g.). The product crystallised from benzene–light petroleum as long colourless rods (1·05 g.), m. p. 161·5—162·5° (corr.) [mixed m. p. 136° with monoacetyl*iso*trichothecolone (m. p. 185—186°)] (Found: C, 67·1, 67·2, 65·5, 65·7; H, 7·3, 7·2, 7·1, 7·0; Ac, 18·6, 18·1, 20·0, 21·7, 23·8. $C_{19}H_{24}O_6$ requires C, 65·5; H, 6·9; 2Ac, 24·7%). The infrared spectrum had max. at 1667 (>CO) and 1742 cm.$^{-1}$ (ester) but no hydroxyl absorption. This compound is believed to be identical with diacetyl*iso*trichothecolone, m. p. 155—157°, obtained on vigorous acetylation by Fishman *et al.*[15] Its 2 : 4-*dinitrophenylhydrazone* separated from ethanol as an amorphous solid, m. p. 155° (corr.) (Found: C, 55·2, 55·6; H, 5·5, 5·5; N, 11·4, 10·9. $C_{25}H_{28}O_9N_4$ requires C, 56·8; H, 5·4; N, 10·6%).

*Diacetyldihydroiso**trichothecolone***.—Under similar conditions dihydro*iso*trichothecolone, m. p. 130—132° (0·8 g.), gave the *diacetate*, m. p. 154—155°, needles from aqueous ethanol (Found: C, 63·3, 63·3; H, 7·3, 7·7; Ac, 31·0, 32·0. $C_{19}H_{26}O_6$ requires C, 65·1; H, 7·5; 2Ac, 24·6%).

Reaction of iso*Trichothecolone with Phosphorus Oxychloride*.—Freshly distilled phosphorus oxychloride (1 ml.) was added to *iso*trichothecolone (0·5 g.) in pyridine (15 ml.). After 20 hr. at room temperature the mixture was diluted with water (100 ml.), and the precipitate collected. Crystallisation from ethanol gave the *product* as colourless needles (0·21 g.) which darkened at 198° but did not give a sharp m. p. (Found: C, 52·3, 52·3; H, 5·3, 5·2; Cl, 10·3, 10·1; P, 9·0. $C_{15}H_{18}O_5PCl$ requires C, 52·3; H, 5·2; Cl, 10·3; P, 9·0%).

iso*Trichothecodione*.—*iso*Trichothecolone dissolved readily in 5% aqueous chromic acid and gradually a colourless crystalline precipitate, m. p. 190—191° (corr.), was obtained. iso-*Trichothecodione* crystallised from benzene in colourless rods (Found: C, 68·3; H, 7·0. $C_{15}H_{18}O_4$ requires C, 68·7; H, 6·9%), $[\alpha]_D^{18}$ −28·8° (*c* 3·0 in ethanol) (*c* 3·0), absorbing 1 mol. of hydrogen. Further oxidation of *iso*trichothecodione with chromic acid in acetic acid gave only a trace of an acid, m. p. 207—209° (corr.), the bulk of the original material being recovered unchanged. *iso*Trichothecodione dissolved readily in a small volume of concentrated hydrochloric acid and was precipitated unchanged on addition of water.

*Acetyliso**trichothecodione***, crystallised from water, had m. p. 184—185° (corr.) (Found: C, 67·2, 67·5; H, 6·6, 6·7; Ac, 13·7. $C_{17}H_{20}O_5$ requires C, 67·1; H, 6·6; Ac, 14·1%), and the 2 : 4-dinitrophenylhydrazone, prepared in low yield by Allen's method, had m. p. 194—195° (corr.).

*Dihydroiso**trichothecodione***.—*iso*Trichothecodione (0·5 g.) in ethanol was hydrogenated at 1 atm. with palladium–charcoal: 1 mol. of hydrogen was absorbed. *Dihydroiso**trichothecodione*** crystallised from benzene as prisms (0·41 g.), m. p. 176—178° (corr.) (Found: C 68·1, 68·2; H, 7·2, 7·5. $C_{15}H_{20}O_4$ requires C, 68·2; H, 7·6%).

*Oxidation of Dihydroiso**trichothecolone***.—Dihydro*iso*trichothecolone (m. p. 132°; 0·5 g.) was treated with chromic acid in acetic acid as previously described. The product crystallised from benzene in compact crystals, m. p. 166—167° (corr.) (Found: C, 57·9, 57·6; H, 7·3, 7·2%; equiv., 310, 306. $C_{15}H_{20}O_6,H_2O$ requires C, 57·3; H, 7·0%; *M*, 314). The *acid* was not decarboxylated at the m. p. With acetic anhydride and pyridine it gave a syrupy *acetate* (Found: C, 60·0, 59·0, 59·3; H, 6·6, 6·6, 6·5; Ac, 11·2. $C_{17}H_{22}O_7$ requires C, 60·4; H, 6·5; Ac, 12·7%). The orange 2 : 4-*dinitrophenylhydrazone* of the acid had m. p. 137° (Found: C, 51·1, 50·9; H, 4·9, 5·3; N, 11·7, 11·8. $C_{21}H_{26}O_{10}N_4$ requires C, 51·0; H, 5·3; N, 11·3%).

*Oxidation of Dihydroiso**trichothecodione***.—The hydrogenation product of *iso*trichothecodione (1·5 g.) in acetic acid (3 ml.) was added to 5% aqueous chromic acid (60 ml.), and the mixture kept at room temperature for 4 days. Extraction with ether gave a colourless acidic solid

which crystallised from benzene in compact crystals (1·28 g.), m. p. 162—163° (corr.), undepressed on admixture with the acid $C_{15}H_{20}O_6.H_2O$, m. p. 166—167°, described above.

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RESEARCH DEPARTMENT, IMPERIAL CHEMICAL INDUSTRIES LIMITED,
NOBEL DIVISION, STEVENSTON, AYRSHIRE.
RESEARCH DEPARTMENT, IMPERIAL CHEMICAL INDUSTRIES LIMITED,
PHARMACEUTICALS DIVISION, ALDERLEY PARK,
MACCLESFIELD, CHESHIRE.

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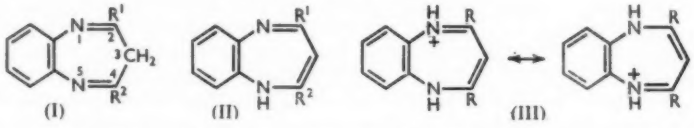
225. *Seven-membered Heterocyclic Compounds. Part I.* 1 : 5-*Benzodiazepines and Derivatives of* 3 : 6-*Diaza*-4 : 5-*benzotropone.*

By J. A. BARLTROP, C. G. RICHARDS, D. M. RUSSELL, and (in part) G. RYBACK.

The chemistry, with particular reference to cationoid attack, of 1 : 5-benzodiazepines (I) is discussed. The transformation of 1 : 5-benzodiazepines into derivatives of 3 : 6-diaza-4 : 5-benzotropone, *e.g.*, (VII; R = N·OH), and the reactions of these systems are described.

THIS investigation was undertaken in order to examine the possibility that there might be a new field of organic chemistry concerned with seven-membered aromatic heterocyclic systems bearing the same relation to pyridine, pyrimidine, etc., as tropone does to benzene. A literature survey suggested that 1 : 5-benzodiazepines (I), readily prepared [1] by condensing *o*-phenylenediamine with β-diketones, were probably the most accessible intermediates for initial experiments.

These substances, though colourless, give rise to intensely purple salts, the colour presumably arising from the resonance canonical forms (III) which are formally analogous to those responsible for the colour of the cyanine dyes.



(I) (II) (III)

Schwarzenbach and Lutz [2] have shown that basification of an aqueous solution of salts containing the cation (III; R = Me) gives, by a very fast reaction, the yellow tautomeric form (II; $R^1 = R^2 = Me$) of the free base which then relatively slowly changes into a colourless form which is either (I; $R^1 = R^2 = Me$) or (IV; R = Me). The free bases, both in the solid state and in organic solvents, exist almost entirely in the di-imino-form (I) because: (i) the infrared spectra of the dimethyl- (I; $R^1 = R^2 = Me$) and the diphenylbenzodiazepine (I; $R^1 = R^2 = Ph$) in Nujol and in $CHCl_3$ show no trace of NH absorption; (ii) the ultraviolet absorption spectrum of the diazepine (I; $R^1 = R^2 = Ph$) is similar to that of benzylideneaniline ($\lambda_{max.}$ 2620, ε 15,500; inflexion 3090 Å, ε 9500) (in EtOH); (iii) the nuclear magnetic resonance spectrum [3] in ethanol of the compound (I; $R^1 = R^2 = Me$) shows only a single absorption band due to the methyl protons, thus indicating a symmetrical molecule: the presence of a CH_2 group in the system is also demonstrated.

It appears that in aqueous solvents also the free bases exist in the di-imino-form, for the ultraviolet absorption spectra of the diphenylbenzodiazepine (I; $R^1 = R^2 = Ph$) in ethanol and in 50% aqueous ethanol are identical (any change in the extinction coefficient of the 258 mμ band is less than 0·2%). For this substance, at least, the evidence is against

[1] Thiele and Steimmig, *Ber.*, 1907, **40**, 955.
[2] Schwarzenbach and Lutz, *Helv. Chim. Acta*, 1940, **23**, 1139.
[3] Barltrop, Richards, and Russell, *J.*, 1959, in the press.

the presence of any detectable amount of the ring-opened form (IV; R = Ph). 1 : 5-Benzodiazepines are unstable systems, their salts in aqueous solution giving reactions characteristic of *o*-phenylenediamine and the β-diketones from which they are derived.

TABLE 1. *Ultraviolet and visible absorption spectra.*

		λ (Å)	ε	λ (Å)	ε
	Quinoxalines				
1	2 : 3-Dimethyl			2370	25900
2	2-Acetyl-3-methyl	2075	28200	2445	32600
3	2-Acetyl-3-methyl oxime	2105	28500	2415	25700
4	2-Acetyl-3-phenyl	2055	31300	2465	34300
5	2-Ethoxycarbonyl-3-phenyl	2135	22800	2435	32700
	1 : 5-*Benzodiazepines*				
6	2 : 4-Dimethyl	2175	25300	2635	6150
7	2 : 4-Dimethyl (hydrogen sulphate) [a]	2240	18500	2595	30200
8	2 : 3 : 4-Trimethyl	2200	25900	2650	6020
9	2 : 3 : 4-Trimethyl (hydrochloride)	2370	15100	2650	20900
10	2 : 4-Diphenyl			2580	45000
11	2 : 4-Diphenyl (hydrochloride)	(2250)	(16500)	(2680)	(21000)
12	2-Methyl-4-phenyl (hydrogen sulphate) [b]	2210	9400	2710	19200
13	2-Methyl-4-*m*-methoxyphenyl (hydrogen sulphate) [b]	2210	14200	2670	17100
14	2-Methyl-4-*p*-methoxyphenyl (hydrogen sulphate) [b]	2300	8900	2670	10800
15	2-Methyl-4-styryl	2100	32600	(2250)	(23000)
16	2-Methyl-4-styryl (hydrochloride)			2750	16800
17	2 : 4-Distyryl			2210	25500
18	2 : 4-Distyryl (hydrochloride)			2820	21100
19	2 : 4-Dimethyl-3-piperonylidene			2580	16300
20	2 : 4-Dimethyl-3-piperonylidene (hydrochloride)				
21	2-Methyl-4-(3 : 4-methylenedioxystyryl)-3-piperonylidene			2540	13700
22	2-Methyl-4-(3 : 4-methylenedioxystyryl)-3-piperonylidene (hydrochloride)				
23	2 : 4-Dimethyl-1-nitroso			2640	14700
24	3-Hydroxyimino-2 : 4-dimethyl	2185	26300		

	λ (Å)	ε	λ (Å)	ε	λ (Å)	ε	λ (Å)	ε	λ (Å)	ε	λ (Å)	ε
1	3160	7200	(3225)	(5600)								
2	3040	6400	(3265)	(5200)								
3	3290	8800	(3465)	(5300)								
4	3315	7400										
5	3315	8500										
6												
7	2685	28400	3255	1150	3345	1100	4940	880	(5735)	(557)	(6315)	(245)
8												
9	2690	20300	(3110)	(1010)			4730	1130				
10	(3350)	(11400)										
11	2910	26600	(3170)	(20000)			5140	1900				
12	3000	13600					5100	1350				
13	2960	12300	3395	5130			5000	1400	5200	1420		
14	2770	10900	3500	10600			5050	1900				
15	3010	31300	(3100)	30200	(3300)	24900						
16	(3460)	(22700)	3740	29100			5480	1440				
17	2990	60000										
18			3970	44000			5800	2800			9030	2210
19	3040	13300	3530	30800								
20	2790	20200	3260	7520	4260	31100						
21	3040	15100	3450	30600								
22	2930	17400	(3030)	(16900)	4390	28700						
23			3090	12000								
24												

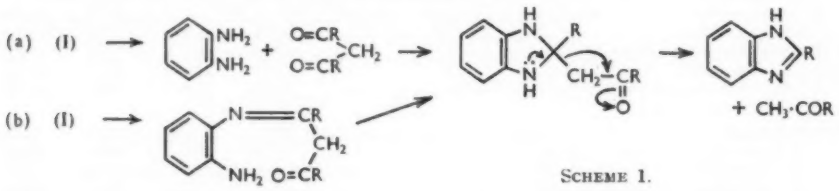
[a] This spectrum was measured on an aqueous solution. [b] These spectra were obtained from methanol solutions.

All other spectra are for solutions in ethanol. Data in parentheses refer to points of inflexion.

For example, salts of 2 : 4-dimethyl-1 : 5-benzodiazepine (I; $R^1 = R^2 = Me$) with diacetyl give 2 : 3-dimethylquinoxaline, and with phenylhydrazine give 3 : 5-dimethyl-1-phenylpyrazole.[1] The diazepinium cations (III; $R^1 = Me$, $R^2 = Me$ or Ph) undergo ring-contraction [1] in warm aqueous solution to the corresponding 2-substituted benziminazoles. Although the simplest picture of these reactions is obtained by postulating complete

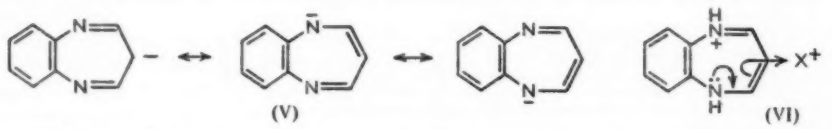
hydrolysis of the diazepine into its components (a, Scheme 1) it seems at least equally probable that the reactions proceed by the fission of one C=N bond only (b, Scheme 1).

On theoretical grounds, one would expect the 1 : 5-benzodiazepines to be susceptible to cationoid attack at position 3, (i) under base-catalysed conditions through the participation of the mesomeric ion (V) and (ii) under acidic conditions through the electromeric displacements (VI). Methyl groups at positions 2 and 4 should also be reactive.



SCHEME 1.

These predictions have experimental support. The diazepine (I; $R^1 = R^2 = Me$), treated in liquid ammonia with sodamide and methyl iodide, gives 2 : 3 : 4-trimethyl-1 : 5-benzodiazepine, m. p. 85°, apparently identical with a compound of m. p. 86° prepared by Vaisman [4] by condensing *o*-phenylenediamine with 3-methylpentane-2 : 4-



dione. That methylation occurred, not on the nitrogen atom, but at position 3 follows from the reaction of the compound with phenylhydrazine which gave *o*-phenylenediamine and 3 : 4 : 5-trimethyl-1-phenylpyrazole.

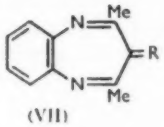
The reaction of the dimethylbenzodiazepine (I; $R^1 = R^2 = Me$) with aromatic aldehydes is more complicated. Benzaldehyde in the presence of aqueous alkali gave a mixture of the methylstyryldiazepine (I; $R^1 = Me$, $R^2 = Ph{\cdot}CH{=}CH$) and the 2 : 4-distyryldiazepine (I; $R^1 = R^2 = Ph{\cdot}CH{=}CH$). In the presence of sodium ethoxide, only the latter compound was obtained. These condensations involving the methyl groups are reversible, for the distyryl partly reverts to the monostyryl derivative on treatment with aqueous alkali. Piperonaldehyde, on the other hand, in the presence of sodium ethoxide or of aqueous alkali, gives the 3-piperonylidene derivative (VII; R = piperonylidene) together with a small amount of the dipiperonylidene derivative (VIII; Ar = $CH_2O_2C_6H_3$).

The positions of the arylidene residues in these compounds were assigned on spectroscopic evidence. Examination of the spectra of all the diazepines in Table 1, which lack a substituent doubly bonded to the 3-position, shows, not only considerable variations in the ultraviolet spectra (which may be partly ascribed to the superimposition on the spectrum of the benzodiazepine nucleus the absorptions due to partial chromophores, *e.g.*, Ph·CH=CH·C=N in Nos. 17 and 18), but also the presence of one common feature—a low-intensity band in the visible region around 5000 Å characteristic of the salts of these compounds and responsible for their intense colours. This feature, which is found in the mono- and di-benzylidene derivatives described above, leads to the suggestion that in these compounds, condensation had occurred on the methyl groups of the dimethylbenzodiazepine. This notion is supported by the infrared spectra of these compounds. The free bases (in Nujol) show strong absorptions at 980 and 967 cm.$^{-1}$ respectively (*trans*-CH=CH-) but have no strong band in the region 840—790 cm.$^{-1}$ expected for >C=CH-. In the electronic spectra of the condensation products with piperonaldehyde, the low-intensity band in the visible region is replaced by a high-intensity band near 4300 Å

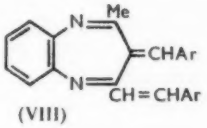
[4] Vaisman, *Trudy Inst. Khim. Kharkov Gosud. Univ.*, 1938, **4**, 157; 1940, **5**, 57; *Chem. Abs.*, 1940, **34**, 5847; 1944, **38**, 750.

(Nos. 20 and 22). This marked change presumably implies a disruption of the resonating system (III) responsible for the colour of 1 : 5-benzodiazepinium salts and, for this reason, a piperonylidene residue is assigned to position 3 in these derivatives.

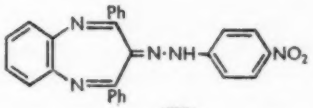
While these compounds are much more stable to hot acid than the parent dimethyldiazepine, the mode of decomposition is similar. The diazepine (VII; R = piperonylidene) gives piperonylideneacetone, 2-methylbenziminazole, and 2-(3 : 4-methylenedioxystyryl)-benziminazole.



(VII)



(VIII)



(IX)

An attempt was also made to prepare the compound (VII; R = Ph·CH=) by condensing *o*-phenylenediamine with 3-benzylidenepentane-2 : 4-dione. With or without acetic acid as catalyst, the product was 2-phenylbenziminazole. With piperidine, 2 : 4-dimethyl-1 : 5-benzodiazepine (I; $R^1 = R^2 = Me$) was obtained, possibly by hydrolysis of the diazepine (VII; R = Ph·CH=). A similar result attended an attempt to prepare 3-acetyl-2 : 4-dimethyl-1 : 5-benzodiazepine by condensing *o*-phenylenediamine with triacetylmethane. Under Thiele and Steimmig's [1] conditions only the dimethyldiazepine was obtained, while heating the components together in benzene afforded a mixture of the dimethyldiazepine, *N*-acetyl-*o*-phenylenediamine, and 2-methylbenziminazole.

Coupling between the *p*-nitrobenzenediazonium cation and the diphenylbenzodiazepine (I; $R^1 = R^2 = Ph$) also occurs in the 3-position, giving what is probably the *p*-nitrophenylhydrazone (IX) of the diphenylbenzotropone. The structure of this compound follows from its infrared spectrum, which shows a NH band. This feature is incompatible with coupling either in the benzene ring or on the NH group of the tautomeric form (II; $R^1 = R^2 = Ph$) of the diazepine. That the substance is the *p*-nitrophenylhydrazone of 2-benzoyl-3-phenylquinoxaline cannot be excluded on present evidence, though the mild conditions of its formation make this unlikely.

1 : 5-Benzodiazepines are clearly not aromatic. The tautomeric form (I) has not the requisite cyclic conjugation and the form (II), though cyclically conjugated, has eight delocalised electrons in its heterocyclic ring (two each from the secondary nitrogen atom and the three double bonds) as against the six required for aromaticity. This lack of aromatic character receives experimental support from the ease with which the nitrogenous ring undergoes fission and ring contraction. By analogy with *cyclo*heptatriene and tropone, aromatic properties might be expected to develop in systems such as (VII; R = O, NR, S, etc.) and the rest of this paper is devoted to a description of experiments on the synthesis of such compounds.

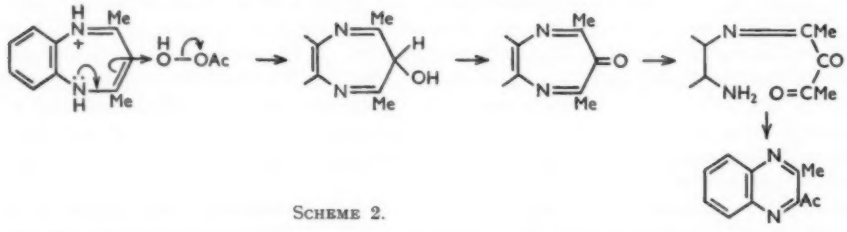
The known susceptibility of 1 : 5-benzodiazepines to cationoid attack suggested that the diazatropone (VII; R = O) might be prepared by oxidising the dimethyldiazepine (I; $R^1 = R^2 = Me$) with per-acids. Both monopersulphuric acid and peracetic acid gave a compound, $C_{11}H_{10}ON_2$, which was found to be identical with a substance which had been prepared [5,6] from *o*-phenylenediamine and pentane-2 : 3 : 4-trione and described as 2-acetyl-3-methylquinoxaline (X). This result alone does not permit a distinction to be made between the 6- and the 7-membered ring formulation. However, we believe the structure (X) to be correct for the following reasons: (i) the carbonyl stretching band in the infrared spectrum lies at 1695 cm.$^{-1}$ in Nujol and 1702 cm.$^{-1}$ in carbon tetrachloride, remote from the 1641 cm.$^{-1}$ band given [7] by 3-benzotropone and near that expected (1700—1680 cm.$^{-1}$) for an aryl methyl ketone; (ii) the ultraviolet spectrum (see Table 1) closely resembles

[5] Piutti, *Gazzetta*, 1936, **66**, 276.
[6] Sachs and Barschall, *Ber.*, 1901, **34**, 3054; Sachs and Röhmer, *Ber.*, 1902, **35**, 3308.
[7] Scott and Tarbell, *J. Amer. Chem. Soc.*, 1950, **72**, 240.

those of authentic quinoxalines; (iii) the nuclear magnetic resonance spectrum [3] of the compound in methanol indicates the presence of two differently situated methyl groups; (iv) a Claisen condensation between ethyl 2-phenylquinoxaline-3-carboxylate and ethyl acetate, followed by hydrolysis of the β-keto-ester, gives a compound identical with that obtained by oxidising 2-methyl-4-phenyl-1 : 5-benzodiazepine with peracetic acid and which from its spectrum and from its method of synthesis must be 2-acetyl-3-phenylquinoxaline.

An interpretation of this oxidative ring-contraction in terms of a hydrolytic equilibrium between the diazepine and acetylacetone, the latter being oxidised to pentane-2 : 3 : 4-trione which then condenses with the diamine to give the acylquinoxaline, seems unlikely since, in a model experiment, no pentanetrione could be isolated on peracetic acid oxidation of acetylacetone, and because, under comparable conditions, peracetic acid reacted with the diazepine many times faster than with acetylacetone. Scheme 2, which postulates the formation and subsequent decomposition of the diazabenzotropone, may be more acceptable, the more so since the diazatropone oxime (VII; R = N·OH) has been shown to undergo an analogous ring-contraction.

A second attempt to prepare derivatives of the diazabenzotropone which involved condensing *o*-phenylenediamine with 3-hydroxyiminopentane-2 : 4-dione was more successful. The components reacted smoothly in benzene to give a compound (A), $C_{11}H_{11}ON_3$, m. p. 215° (decomp.), which must be formulated as the diazabenzotropone oxime (VII; R = N·OH) or as the *cis*- or *trans*-form (XI) of the oxime of 2-acetyl-3-methylquinoxaline, the infrared spectrum indicating the presence of an acidic OH group.



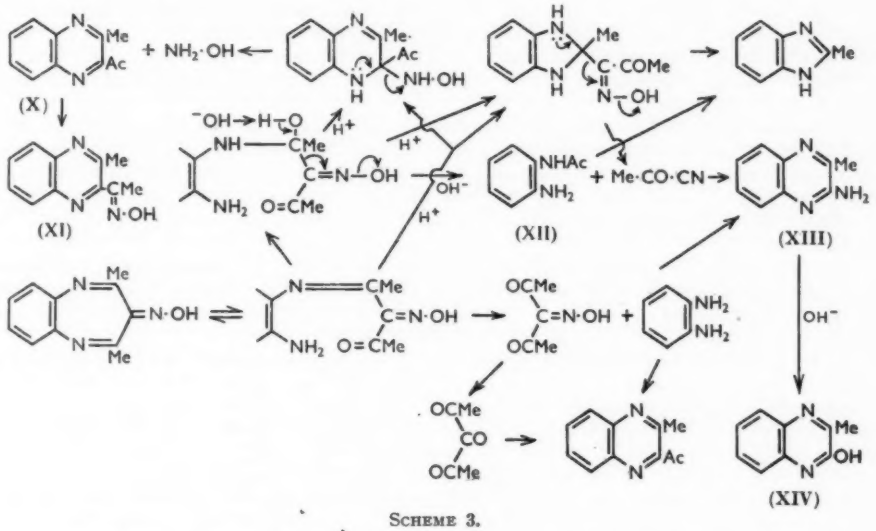
SCHEME 2.

An oxime B, m. p. 196°, of acetylmethylquinoxaline, prepared from the ketone by standard methods, failed to form a chelate compound with cupric acetate and is therefore the form with the N·OH group oriented *anti* with respect to the quinoxaline nucleus. The oxime A although different from this oxime is nevertheless readily transformed into it by treatment with dilute acids. The ultraviolet (see Table 1) and infrared spectra of the oximes A and B differ so profoundly that it is virtually certain that the two compounds cannot be *cis–trans*-isomers and we are led to the conclusion that oxime A is in fact the diazabenzotropone oxime (VII; R = N·OH), a conclusion supported by the pronounced differences in the chemistry of the oximes A and B. Thus, the oxime A on treatment with acetylacetone in the presence of dilute sulphuric acid (but not acetic acid) gives 2 : 4-dimethyl-1 : 5-benzodiazepine sulphate. A similar transformation could not be effected with oxime B.

All attempts to hydrolyse the diazabenzotropone oxime to the diazatropone have been vitiated by ring-contraction. Mineral acids gave oxime B and 2-acetyl-3-methylquinoxaline, while oxalic acid and even acetic acid converted the substance into oxime B and 2-methylbenziminazole.

The diazabenzotropone oxime is also unstable to alkaline reagents. With sodium hydroxide solution it decomposes to, *inter alia*, *o*-phenylenediamine, 2-methylbenziminazole, and 2-hydroxy-3-methylquinoxaline (XIV). With hot sodium carbonate solution it gives the same three products and also *N*-acetyl-*o*-phenylenediamine (XII) and 2-amino-3-methylquinoxaline (XIII). All these transformations may be rationalised in terms of the

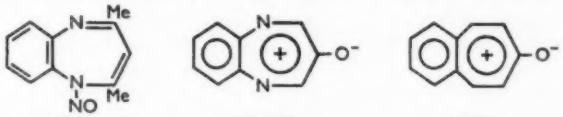
reactions of Scheme 3. The hydroxymethylquinoxaline (XIV) is presumably derived from the aminomethylquinoxaline (XIII) since the latter can be slowly converted into the former by boiling alkali.



SCHEME 3.

An attempt to prepare the diazabenzotropone oxime (VII; R = N·OH) by treating the dimethylbenzodiazepine (I; $R^1 = R^2 = Me$) with sodium nitrite in acetic acid gave, instead, 2-methylbenziminazole and 2-acetyl-3-methylquinoxaline, these compounds presumably being formed through the known rearrangement, by the acetic acid present, of the diazabenzotropone oxime first formed. 2 : 4-Dimethyl-1-nitroso-1 : 5-benzodiazepine (XV) was also formed in this reaction. Its structure is proved by its failure to give intensely coloured salts with acids as would be expected of isomers in which the nitroso-group was located on a methyl group or at position 7, and by its infrared absorption at 1680 cm.$^{-1}$ (in Nujol) (N–N=O; cf. nitrosoguanidine [8] 1653 cm.$^{-1}$). Ozonolysis of the piperonylidene derivative (VII; R = piperonylidene) also failed to yield the required diazabenzotropone—piperonaldehyde was the only identifiable product.

It is quite clear from these results that diazabenzotropone and its derivatives are much more unstable than 3-benzotropone. This is to be expected. Since the ionisation potential of nitrogen is higher than that of carbon, aromatic structures such as (XVI) will be less stable than the corresponding benzotropone structures such as (XVII).



(XV) (XVI) (XVII)

EXPERIMENTAL

2 : 4-*Dimethyl*-1 : 5-*benzodiazepine*.—Acetylacetone (18 c.c.) was added in portions with shaking to a warm solution of *o*-phenylenediamine (19 g.) in ethanol (70 c.c.) and acetic acid (30 c.c.). Concentrated sulphuric acid (25 c.c.) diluted with a little water was added to the violet solution. The precipitated *sulphate* (40 g., 90%) was collected, washed with ethanol and

[8] Lieber, Levering, and Patterson, *Analyt. Chem.*, 1951, **23**, 1594.

with ether, and dried. It formed black-violet needles, m. p. 226° (Found: C, 49·3; H, 5·2; N, 10·8. $C_{11}H_{12}N_2,H_2SO_4$ requires C, 48·9; H, 5·2; N, 10·4%).

2-Methyl-4-phenyl-1 : 5-benzodiazepine (cf. ref. 1).—A solution of *o*-phenylenediamine (2 g.) and benzoylacetone (4 g.) in warm ethanol (8 c.c.) and acetic acid (3 c.c.) was kept at 40° for 30 min., cooled, diluted with ether (20 c.c.), and treated with concentrated sulphuric acid (2·5 c.c.) in water (5 c.c.). The *diazepine hydrogen sulphate monohydrate* (4·9 g., 75%) which separated overnight was collected, washed well with ether, and dried *in vacuo*. It had m. p. 173—175° (Found: C, 54·8; H, 5·1; N, 7·95; S, 9·2. $C_{16}H_{14}N_2,H_2SO_4,H_2O$ requires C, 54·8; H, 5·1; N, 8·0; S, 9·1%).

2-m-*Methoxyphenyl-4-methyl-1 : 5-benzodiazepine.*—A solution of *o*-phenylenediamine (0·12 g.) and *m*-methoxybenzoylacetone (0·3 g.) in ethanol (2 c.c.) and acetic acid (1 c.c.) was kept at 40° for 90 min. The solution, when cool, was treated with 30% sulphuric acid (4 drops), then cautiously diluted with ether. The *diazepine hydrogen sulphate* (0·19 g.; m. p. 163°), which separated as violet crystals, was collected, washed with ether and dried *in vacuo* (Found: C, 56·0; H, 4·9; N, 7·6; S, 8·6. $C_{17}H_{16}ON_2,H_2SO_4$ requires C, 56·3; H, 5·0; N, 7·7; S, 8·9%).

2-p-*Methoxyphenyl-4-methyl-1 : 5-benzodiazepine.*—A solution of *p*-methoxybenzoylacetone (1 g.) and *o*-phenylenediamine (0·5 g.) in ethanol (6 c.c.) and acetic acid (1 c.c.) was kept at 40° for 4 hr., then worked up as above. The *diazepine hydrogen sulphate* was obtained as dark violet crystals (1·46 g., 86%), m. p. 191° (Found: C, 55·6; H, 4·8%).

2 : 4-Diphenyl-1 : 5-benzodiazepine [with G. R.].—*o*-Phenylenediamine (21·6 g.), dibenzoylmethane (44·8 g.), toluene-*p*-sulphonic acid (1·0 g.) and dry xylene (200 c.c.) were boiled together under a Dean–Stark head for 4 hr. and then cooled. 2-Phenylbenziminazole (10 g.), contaminated with a little diphenylbenzodiazepine, separated, having m. p. 287—289° (from methanol) (Found: C, 80·2; H, 5·2; N, 14·7. Calc. for $C_{13}H_{10}N_2$: C, 80·4; H, 5·2; N, 14·4%). Concentration of the filtrate gave the *diphenylbenzodiazepine* (27·0 g., 45%) which formed colourless needles, m. p. 140°, from methanol (Found: C, 85·3; H, 5·6; N, 9·5. $C_{21}H_{16}N_2$ requires C, 85·1; H, 5·4; N, 9·5%), ν (in CS_2) 2900 cm.$^{-1}$ (CH_2), no NH band. The *hydrochloride trihydrate*, m. p. 242—244° (decomp.), was obtained as a violet powder when the hydrochloride, prepared in ether, was dried in air (Found: C, 64·8; H, 5·7; N, 7·1. $C_{21}H_{16}N_2,HCl,3H_2O$ requires C, 65·1; H, 6·0; N, 7·2%). The *hydrochloride monohydrate*, blue-black needles, m. p. 242—244° (decomp.), was obtained by evaporating a solution of the trihydrate in ethanol over sulphuric acid in a desiccator, followed by drying at 78° *in vacuo* (Found: C, 71·2; H, 5·4; N, 8·1; Cl, 10·3. $C_{21}H_{16}N_2,HCl,H_2O$ requires C, 71·8; H, 5·5; N, 8·0; Cl, 10·1%). The *hydrobromide hemihydrate*, a black powder, m. p. 221° after drying *in vacuo* at 110°, was prepared in ethanol and crystallised from ethanol–ether (Found: C, 64·8; H, 4·8; N, 7·5; Br, 20·4. $C_{21}H_{16}N_2,HBr,\frac{1}{2}H_2O$ requires C, 65·1; H, 4·7; N, 7·3; Br, 20·7%). The *picrate* formed coppery-brown needles, m. p. 216—217°, from methanol (Found: C, 60·5; H, 4·1. $C_{21}H_{16}N_2,C_6H_3O_7N_3,CH_3{\cdot}OH$ requires C, 60·3; H, 4·2%).

Condensations effected in ethanolic acetic acid (cf. Thiele and Steimmig [1]) gave much smaller yields.

Reaction of 2 : 4-Dimethyl-1 : 5-benzodiazepine with Diacetyl.—The diazepine hydrogen sulphate (2 g.) in water (100 c.c.) was shaken with diacetyl (1 c.c.) for 65 hr. until the purple colour had disappeared. 2 : 3-Dimethylquinoxaline (1·05 g.), m. p. 104—106°, was obtained by isolation with ether and distillation of the excess of diacetyl. Recrystallisation from water gave a specimen (0·8 g.), m. p. 106° alone and when mixed with authentic material. The compound and 2 : 3-dimethylquinoxaline had identical infrared spectra.

2-Acetyl-3-methylquinoxaline.—(*A*) A solution of monopersulphuric acid was prepared by dissolving potassium dipersulphate (13 g.) in concentrated sulphuric acid (16 c.c.) and, after an interval, diluting the mixture with water (40 c.c.). A solution of 2 : 4-dimethyl-1 : 5-benzodiazepine hydrogen sulphate (5 g.) in water (50 c.c.) was added with stirring. When the purple colour had faded (*ca.* 3 hr.), the mixture was basified with sodium hydroxide solution and cooled and the precipitated solid was collected, washed, and dried. 2-Acetyl-3-methylquinoxaline (0·4 g., 12%) crystallised from aqueous ethanol in colourless needles, m. p. and mixed m. p. 87°, giving an intense yellow colour with concentrated sulphuric acid (Found: C, 70·3; H, 5·2; N, 15·2. Calc. for $C_{11}H_{10}ON_2$: C, 71·0; H, 5·4; N, 15·1%). The phenylhydrazone formed needles, m. p. 176°, giving a blue colour in concentrated sulphuric acid. Sachs and Barschall [6] give m. p. 86·5° for the ketone, and Sachs and Röhmer [6] give m. p. 178° for the phenylhydrazone and the same colour reactions. The *2 : 4-dinitrophenylhydrazone* separated from

acetic acid as orange-red plates m. p. 246—247° (Found: C, 55·4; H, 4·0; N, 23·8. $C_{17}H_{14}O_4N_6$ requires C, 55·7; H, 3·9; N, 23·0%), the oxime as prisms (from aqueous ethanol), m. p. 196° (Found: C, 65·6; H, 5·5; N, 20·4. Calc. for $C_{11}H_{11}ON_3$: C, 65·7; H, 5·5; N, 20·9%) (Sachs and Röhmer [8] give m. p. 194·5°), and the *semicarbazone* as plates, m. p. 247°, from aqueous ethanol (Found: N, 28·6. $C_{12}H_{13}ON_5$ requires N, 28·8%).

(*B*) 12·5% Peracetic acid in acetic acid (450 c.c.) was added slowly to 2 : 4-dimethyl-1 : 5-benzodiazepine hydrogen sulphate (60 g.) dissolved in water (1 l.). After being warmed slightly, the mixture was set aside overnight, then basified and extracted with chloroform. The extracts were dried and evaporated and the residual gum was sublimed at 130—140°/15 mm. The sublimate, crystallised from aqueous ethanol, gave 2-acetyl-3-methylquinoxaline (11 g.), m. p. 87°, alone and when mixed with specimens prepared as above and in accordance with Piutti's directions.[5]

2-*Acetyl*-3-*phenylquinoxaline*.—(*A*) 2-Methyl-4-phenyl-1 : 5-benzodiazepine hydrogen sulphate monohydrate (4 g.) in water (125 c.c.) was oxidised for 3 hr. with peracetic acid solution as described for the previous compound. 2-Acetyl-3-phenylquinoxaline was isolated with chloroform, sublimed at 140—150°/15 mm., and crystallised from ethanol. It formed needles (0·7 g., 35%), m. p. 110° (Found: C, 76·8; H, 4·8; N, 10·9. Calc. for $C_{16}H_{12}ON_2$: C, 77·4; H, 4·9; N, 11·3%). Sachs and Röhmer [8] give m. p. 99·5°; Lutz and Stuart [9] give m. p. 110—111°. The 2 : 4-*dinitrophenylhydrazone* separated from acetic acid in orange-red plates m. p. 223° (Found: C, 61·8; H, 4·0; N, 19·1. $C_{22}H_{16}O_4N_6$ requires C, 61·7; H, 3·8; N, 19·6%).

(*B*) A mixture of ethyl 2-phenylquinoxaline-3-carboxylate (5 g.), ethyl acetate (50 c.c.), and sodium wire (2 g.) was boiled under reflux for 7 hr., poured into ice and dilute hydrochloric acid, and extracted with ether. Distillation of the extracts gave acetoacetic ester (5 c.c.) and a residual gum which was dissolved in ethanol (25 c.c.), boiled under reflux for 18 hr. with concentrated hydrochloric acid (25 c.c.) and water (25 c.c.), diluted with water, and extracted with ether. The extract was washed with 2N-sodium hydroxide solution, dried, and evaporated, and the residue sublimed at 170—190°/15 mm. The sublimate, a mixture of 2-phenylquinoxaline and 2-acetyl-3-phenylquinoxaline (2·54 g.), was dissolved in light petroleum and chromatographed over alumina (170 g.). 2-Phenylquinoxaline (1·78 g.), which came off the column first, when crystallised from light petroleum (b. p. 40—60°), formed crystals (1·45 g.), m. p. 77—78° (Found: C, 81·8; H, 4·8; N, 13·1. Calc. for $C_{14}H_{10}N_2$: C, 81·5; H, 4·9; N, 13·6%). Fischer and Römer [10] give m. p. 78°. Further development of the column with light petroleum gave 2-acetyl-3-phenylquinoxaline (0·73 g.), which separated from light petroleum (b. p. 40—60°) in crystals (0·62 g.), m. p. and mixed m. p. 111—112° (Found: C, 77·1; H, 4·9; N, 11·7. Calc. for $C_{16}H_{12}ON_2$: C, 77·4; H, 4·9; N, 11·3%). The sodium hydroxide washings when acidified and extracted with ether gave 2-hydroxy-3-phenylquinoxaline, which when recrystallised from aqueous ethanol gave crystals (0·62 g.), m. p. 252° (Buraczewski and Marchlewski [11] give m. p. 247°) (Found: C, 75·7; H, 4·9; N, 12·3. Calc. for $C_{14}H_{10}ON_2$: C, 75·7; H, 4·5; N, 12·6%).

2 : 3 : 4-*Trimethyl*-1 : 5-*benzodiazepine*.—2 : 4-Dimethyl-1 : 5-benzodiazepine (3 g.) in dry tetrahydrofuran (20 c.c.) was added to a stirred solution of sodamide [from sodium (0·4 g.)] in liquid ammonia (150 c.c.), and after 15 min. methyl iodide (5·0 g.) was added dropwise. The stirring was continued for a further 15 min. and the ammonia was allowed to evaporate. The residue was treated with water and the product, an oil (3·01 g.) which crystallised, was isolated with ether. Sublimation at 85—90°/0·05 mm. gave the trimethylbenzodiazepine (2·74 g.), m. p. 85°, from light petroleum (Found: C, 76·9; H, 7·8; N, 15·5. Calc. for $C_{12}H_{14}N_2$: C, 77·4; H, 7·6; N, 15·0%).

Reaction of 2 : 3 : 4-*Trimethyl*-1 : 5-*benzodiazepine with Phenylhydrazine*.—The diazepine (470 mg.) in ethanol (10 c.c.) was shaken with a solution of phenylhydrazine (0·25 c.c.) in concentrated hydrochloric acid (0·2 c.c.) and water (5 c.c.) until the deep red colour was discharged (2 hr.), then poured into water. Isolation with ether gave an oil, which on distillation at 195—200° (bath temp.)/24 mm. gave 3 : 4 : 5-trimethyl-1-phenylpyrazole (250 mg.) [picrate (from ethanol), m. p. 115° (lit.,[12] m. p. 116°)]. The aqueous solution, after basification and extraction

[9] Lutz and Stuart, *J. Amer. Chem. Soc.*, 1937, **59**, 2316.
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with ether, gave an oil, which on sublimation at 120—130°/20 mm. afforded *o*-phenylenediamine (110 mg.), m. p. and mixed m. p. 101—102° (from benzene–light petroleum).

Reaction of 2 : 4-*Dimethyl*-1 : 5-*benzodiazepine with Piperonaldehyde.*—(*A*) The diazepine (5·0 g.), piperonaldehyde (4·35 g.), and dry ethanol (150 c.c.) were boiled together for 40 min. in the presence of sodium ethoxide (from sodium, 0·66 g.). After ethanol (50 c.c.) had been distilled, the boiling mixture was filtered. 2-*Methyl*-4-(3 : 4-*methylenedioxystyryl*)-3-*piperonylidene*-1 : 5-*benzodiazepine* (670 mg.) was collected and crystallised from benzene, from which it separated in yellow needles, m. p. 257—258° (Found: C, 74·1; H, 4·7; N, 6·5. $C_{27}H_{20}O_4N_2$ requires C, 74·3; H, 4·6; N, 6·4%), ν (in Nujol) 1627 cm.$^{-1}$. The substance gives a dark brown colour with acids. The filtrate, when kept overnight, deposited yellow 2 : 4-*dimethyl*-3-*piperonylidene*-1 : 5-*benzodiazepine* (2·74 g.), m. p. 192—193° (from benzene–light petroleum) (Found: C, 75·0; H, 5·2; N, 8·9. $C_{19}H_{16}O_2N_2$ requires C, 75·0; H, 5·3; N, 9·2%), ν (in Nujol) 1628 cm.$^{-1}$. The substance gives a dark brown colour with acid.

(*B*) The diazepine (2·0 g.) and aldehyde (1·74 g.) in ethanol (100 c.c.) were set aside for 20 days in the presence of saturated aqueous potassium hydroxide solution (0·3 c.c.), then diluted with water. The product, when isolated with ether and chromatographed in 1 : 1 benzene–light petroleum on alumina, gave piperonaldehyde (460 mg.), 2 : 4-dimethyl-3-piperonylidene-1 : 5-benzodiazepine (1·85 g.), and the dipiperonylidene derivative (40 mg.).

Reaction of 2 : 4-*Dimethyl*-1 : 5-*benzodiazepine with Benzaldehyde.*—(*A*) The diazepine (5 g.) and benzaldehyde (3·1 c.c.) in ethanol (100 c.c.) were boiled under reflux for 1 hr. in the presence of sodium ethoxide (from sodium 0·66 g.). Benzaldehyde (3·1 c.c.) was added and boiling was continued for a further 3 hr. The mixture was concentrated to small bulk, then poured into water, and the oily product (10·5 g.) was isolated with ether and chromatographed on alumina (400 g.) in 1 : 1 benzene–light petroleum. The oil (4·94 g.) so obtained when crystallised from benzene–light petroleum gave 2 : 4-*distyryl*-1 : 5-*benzodiazepine* (2·29 g.), yellow needles, m. p. 164—165° (Found: C, 86·2; H, 5·9; N, 7·8. $C_{25}H_{20}N_2$ requires C, 86·2; H, 5·8; N, 8·0%), ν (in Nujol) 1628 cm.$^{-1}$ (C=C). The substance gives a green solution in acids.

(*B*) The diazepine (6 g.) and benzaldehyde (3·6 c.c.) in ethanol (200 c.c.) were kept for 18 days in the presence of saturated aqueous potassium hydroxide (1 c.c.). The oily product, isolated as in previous experiments, was chromatographed on alumina (600 g.) in 1 : 1 benzene–light petroleum, thus yielding 2 : 4-distyryl-1 : 5-benzodiazepine (2·55 g.), m. p. 164—165° after crystallisation, followed by a sticky solid (3·01 g.) which when crystallised from benzene–light petroleum gave 2-*methyl*-4-*styryl*-1 : 5-*benzodiazepine* (2·14 g.), m. p. 128—129° (Found: C, 82·7; H, 5·9; N, 11·0. $C_{18}H_{16}N_2$ requires C, 83·0; H, 6·2; N, 10·8%), ν (in Nujol) 1630 cm.$^{-1}$. The substance gives a purple colour with acids.

Hydrolysis of 2 : 4-*Distyryl*-1 : 5-*benzodiazepine.*—The diazepine (500 mg.) in ethanol (30 c.c.) was set aside for 8 days with saturated aqueous potassium hydroxide (0·3 c.c.). The product, in 1 : 1 benzene–light petroleum, was chromatographed on alumina, giving successively starting material (130 mg.) and 2-methyl-4-styryl-1 : 5-benzodiazepine (100 mg.), m. p. 128—129° (from benzene–light petroleum).

Reaction of 2 : 4-*Dimethyl*-3-*piperonylidene*-1 : 5-*benzodiazepine with Acid.*—The diazepine (500 mg.) in ethanol (20 c.c.) was heated under reflux with concentrated hydrochloric acid (0·15 c.c.) until the dark brown colour faded (18 hr.). The solution was basified and the solid obtained by isolation with ether was triturated with benzene (15 c.c.). The insoluble material gave 2-(3 : 4-*methylenedioxystyryl*)*benziminazole* (55 mg.), m. p. 220—221° (from aqueous methanol) (Found: C, 73·0; H, 4·8; N, 10·5. $C_{16}H_{12}O_2N_2$ requires C, 72·7; H, 4·6; N, 10·6%). The infrared spectrum (in Nujol) showed the typical broad associated NH band of benziminazoles and a peak at 1255 s cm.$^{-1}$ (aryl ether). The benzene-soluble material was separated by crystallisation from benzene–light petroleum into 2-methylbenziminazole (90 mg.), m. p. and mixed m. p. 174—175°, and piperonylideneacetone (60 mg.), m. p. and mixed m. p. 110°.

Condensation of Benzylideneacetylacetone with o-*Phenylenediamine.*—Benzylideneacetylacetone (5 g.) and *o*-phenylenediamine (2·87 g.) in benzene (60 c.c.) were heated under reflux for 4 hr. with piperidine (0·3 c.c.). Distillation of solvent gave an oil which, chromatographed on alumina in 1 : 1 benzene–light petroleum, gave successively a semi-solid oil (3·31 g.) which yielded 2-phenylbenziminazole (1·15 g.), m. p. 287—289° (from aqueous methanol), and an oil (1·32 g.) which afforded 2 : 4-dimethyl-1 : 5-benzodiazepine (620 mg.), m. p. and mixed m. p. 131—132°, on crystallisation from benzene–light petroleum.

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Similar condensations effected either in boiling toluene without catalyst, or in ethanol–acetic acid at 50°, gave only 2-phenylbenziminazole and *o*-phenylenediamine.

Condensation of o-*Phenylenediamine with Triacetylmethane.*—(*A*) Triacetylmethane (2·5 g.) in ethanol (5 c.c.) and a solution of *o*-phenylenediamine (1·9 g.) in ethanol (7 c.c.) and acetic acid (3 c.c.) were mixed and the resulting violet solution was poured into sulphuric acid (2·5 c.c.) in water (30 c.c.). After 1 hr., 2 : 4-dimethyl-1 : 5-benzodiazepine sulphate (1·44 g.) was collected. It was characterised as the free base, m. p. and mixed m. p. 131—132°.

(*B*) Triacetylmethane (1·5 g.) and *o*-phenylenediamine (1·16 g.) in benzene (75 c.c.) were boiled under reflux for 1½ hr., concentrated to small bulk, then poured into water, and the product, an oil (1·99 g.), was isolated with ether. The oil, washed with 1 : 1 benzene–light petroleum (100 c.c.) left as an insoluble residue *N*-acetyl-*o*-phenylenediamine (250 mg.), m. p. and mixed m. p. 132—133°. The washings, chromatographed on alumina and eluted with benzene, gave 2 : 4-dimethyl-1 : 5-benzodiazepine (350 mg.). Elution with ether gave an oil, which when rechromatographed on alumina and eluted with benzene gave 2-methylbenziminazole (130 mg.), m. p. and mixed m. p. 174—175°. Elution with ether then gave more *N*-acetyl-*o*-phenylenediamine (255 mg.).

3-*Oxo*-2 : 4-*diphenyl*-1 : 5-*benzodiazepine* p-*Nitrophenylhydrazone* [with G. R.].—*p*-Nitroaniline (0·23 g.) in concentrated hydrochloric acid (1 c.c.) and water (5 c.c.) was diazotised at 0° and poured into an ice-cold solution of diphenylbenzodiazepine (0·5 g.) in ethanol (100 c.c.), then treated with a solution of sodium acetate (1·0 g.). Dilution with water gave a brown flocculent precipitate (0·59 g.), which was collected, washed with water, and chromatographed on alumina. Elution with 1 : 10 benzene–light petroleum gave unchanged diphenylbenzodiazepine (0·27 g.). 1 : 1 Benzene–light petroleum eluted the p-*nitrophenylhydrazone* (0·26 g.), a yellow powder (from aqueous ethanol), m. p. 252—253° (Found: C, 73·0; H, 4·8; N, 15·7. $C_{27}H_{19}O_2N_5$ requires C, 72·8; H, 4·3; N, 15·7%), ν (in Nujol) 3300 cm.$^{-1}$ (NH), which gives a yellow colour with hydrochloric acid.

3-*Hydroxyimino*-2 : 4-*dimethyl*-1 : 5-*benzodiazepine.*—*o*-Phenylenediamine (40 g.) and 3-hydroxyiminopentane-2 : 4-dione (40 g.) were refluxed in benzene (400 c.c.) for 1 hr. The *diazatropone oxime* (60 g.), which separated on cooling, was collected and crystallised from methanol. It formed colourless needles, m. p. 215° (decomp.) (Found: C, 65·5; H, 5·5; N, 20·2. $C_{11}H_{11}ON_3$ requires C, 65·7; H, 5·5; N, 20·9%).

Reaction between Acetylacetone and 3-*Hydroxyimino*-2 : 4-*dimethyl*-1 : 5-*benzodiazepine.*—A solution of the oxime (0·5 g.) and acetylacetone (2 c.c.) in ethanol (20 c.c.) at 50° was treated with 2N-sulphuric acid (10 c.c.). An intense purple colour developed immediately. Next morning, the solution was diluted with water (50 c.c.) and washed with ether. The aqueous solution contained 2 : 4-dimethyl-1 : 5-benzodiazepine, identified spectroscopically ($\lambda_{max.}$ 4940 with inflexions at 6315 and 5735 Å) and by boiling the solution until colourless, whereafter basification of the solution followed by isolation with ether gave 2-methylbenziminazole (200 mg.), m. p. 174°, after crystallisation from benzene–ligroin.

Acid Hydrolysis of 3-*Hydroxyimino*-2 : 4-*dimethyl*-1 : 5-*benzodiazepine.*—(*A*) The oxime (2 g.) was heated for 30 min. on the steam-bath with 10% sulphuric acid (120 c.c.) and ferric chloride (1·6 g.), then cooled and extracted with ether. The extracts yielded a gum which was sublimed. 2-Acetyl-3-methylquinoxaline (0·4 g.) was isolated at 130—140°/15 mm.; it had m. p. and mixed m. p. 87° (from aqueous ethanol). Sublimation at 170—180°/15 mm. gave 2-acetyl-3-methylquinoxaline oxime (0·3 g.), m. p. and mixed m. p. 196° (from ethanol).

(*B*) The oxime (500 mg.) in ethanol (15 c.c.) and acetic acid (15 c.c.) was kept at room temperature for 30 hr., then poured into water and extracted with ether. The extract was washed with sodium carbonate solution and evaporated and the product was sublimed at 170—180°/17 mm. 2-Acetyl-3-methylquinoxaline oxime (130 mg.), was obtained having m. p. and mixed m. p. 196° (from aqueous methanol). Basification of the aqueous solution and isolation with ether gave 2-methylbenziminazole (80 mg.), m. p. and mixed m. p. 174—175° (from benzene).

Alkaline Hydrolysis of 3-*Hydroxyimino*-2 : 4-*dimethyl*-1 : 5-*benzodiazepine.*—(*A*) Sodium hydroxide (2·5 g.) and the oxime (5 g.) in water (100 c.c.) were heated on the steam-bath for 17 hr. Ammonia was evolved during the reaction. The solution was extracted with ether, yielding a solid (1·75 g.) which was dissolved in 1 : 1 benzene–light petroleum and chromatographed on alumina. This gave, successively, an orange primary amine (40 mg.), m. p. 135—136° (from benzene–light petroleum), *o*-phenylenediamine (950 mg.), and 2-methylbenziminazole

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(350 mg.). The aqueous reaction mixture, when acidified and extracted with ether, gave a brown solid, which on sublimation at 180—190°/15 mm. and crystallisation from aqueous methanol gave 2-hydroxy-3-methylquinoxaline (70 mg.), m. p. 240—242° (Hinsberg [13] gives m. p. 245°) (Found: C, 67·1; H, 5·1; N, 17·0. Calc. for $C_9H_8ON_2$: C, 67·5; H, 5·0; N, 17·5%), ν (in Nujol) 1668 cm.$^{-1}$. 2-Hydroxy-3-phenylquinoxaline has ν 1665 cm.$^{-1}$.

(*B*) The oxime (5 g.) in ethanol (120 c.c.), and sodium carbonate (3·75 g.) dissolved in water (150 c.c.), were heated together on a steam-bath for 2 hr., then cooled. The solid product (2·35 g.) was isolated with ether and extracted with boiling benzene (100 c.c.), giving 2-methylbenziminazole (740 mg.) as an insoluble residue. The benzene extract was adsorbed on an alumina column. Elution with 1 : 1 benzene–light petroleum gave a mixed fraction from which *o*-phenylenediamine (40 mg.), m. p. and mixed m. p. 101—102°, sublimed at 120—130°/20 mm., leaving as an involatile residue 2-amino-3-methylquinoxaline (320 mg.), m. p. and mixed m. p. 166—167° (from benzene–light petroleum) (Found: C, 67·5; H, 6·0; N, 25·9. Calc. for $C_9H_9N_3$: C, 67·9; H, 5·7; N, 26·4%), ν (in Nujol) 3470, 3300 cm.$^{-1}$ (NH_2). Continued elution gave more aminomethylquinoxaline (350 mg.). Elution with 1 : 10 ether–benzene gave 2-methylbenziminazole (240 mg.), m. p. and mixed m. p. 174—175°, 2-hydroxy-3-methylquinoxaline (90 mg.), m. p. 240—242°, and *N*-acetyl-*o*-phenylenediamine (90 mg.), m. p. and mixed m. p. 132—133° (from benzene–light petroleum).

Hydrolysis of 2-*Amino*-3-*methylquinoxaline*.—The quinoxaline (170 mg.) in ethanol (10 c.c.) was heated on the steam-bath with 2N-sodium hydroxide (5 c.c.) for 3 hr. Starting material (140 mg.) was isolated with ether. The aqueous solution, when acidified and extracted with ether, yielded 2-hydroxy-3-methylquinoxaline (15 mg.), m. p. and mixed m. p. 240—242°, infrared spectrum identical with that of an authentic specimen. Similar results were obtained from a hydrolysis performed with aqueous sodium carbonate.

Nitrosation of 2 : 4-*Dimethyl*-1 : 5-*benzodiazepine*.—Sodium nitrite (1·86 g.) in water (15 c.c.) was added with stirring to the diazepine (2 g.) in ethanol (40 c.c.) and acetic acid (25 c.c.) at 5°. After 10 days at room temperature, the mixture was basified with sodium carbonate solution, and the product isolated with ether, dissolved in 1 : 1 benzene–light petroleum, and chromatographed on alumina. Elution with this solvent gave 2-acetyl-3-methylquinoxaline (300 mg.), m. p. and mixed m. p. 86° (from light petroleum), followed by 2 : 4-*dimethyl*-1-*nitroso*-1 : 5-*benzodiazepine* (180 mg.), pale yellow needles, m. p. 80° (from light petroleum) (Found: C, 65·6; H, 5·7; N, 20·9. $C_{11}H_{11}ON_3$ requires C, 65·7; H, 5·5; N, 20·9%). The latter substance gives a yellow solution with acids. Elution with ether yielded 2-methylbenziminazole (270 mg.), m. p. and mixed m. p. 174—175°.

Ozonolysis of 2 : 4-*Dimethyl*-3-*piperonylidene*-1 : 5-*benzodiazepine*.—The diazepine (500 mg.) in ethyl acetate (20 c.c.) and acetic acid (30 c.c.) was ozonised at 0° with 2% ozonised oxygen containing 1·6 mol. of ozone. The solution was flushed with nitrogen, water (30 c.c.) was added, and after 18 hr. the mixture was diluted with water and extracted with ether. The ether extract, on chromatography, gave only piperonaldehyde (50 mg.), identified as the 2 : 4-dinitrophenylhydrazone, m. p. 275—277° (decomp.) (from acetic acid). The aqueous reaction mixture when basified and extracted with ether gave only unchanged diazepine (80 mg.).

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Dyson Perrins Laboratory, Oxford University. [*Received, October 1st*, 1958.]

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226. *Derivatives of 4-Ethoxycarbonyl- and 4-Hydroxy-4-phenylpiperidine.*

By B. G. Boggiano, V. Petrow, O. Stephenson, and A. M. Wild.

By condensation of 3-aryloxy-1 : 2-epoxypropanes with the bases (I; R = H) and (I*a*; R = H), the corresponding 3-aryloxy-2-hydroxypropyl derivatives were readily prepared. 4-Hydroxy-4-phenylpiperidine (I*b*; R = R″ = H) likewise yielded the *N*-(2-hydroxy-3-phenoxypropyl) derivative, but all attempts to convert this compound into the 4-monopropionate proved unsuccessful.

During studies of aryloxyhydroxypropyl amines we found that attachment of the 3-aryloxy-2-hydroxypropyl residue (II) on to the nitrogen atom of cyclic amines such as 1 : 2 : 3 : 6-tetrahydropyridine leads to compounds with significant analgesic activity.[1] In seeking to obtain more potent analgesics, we have condensed a series of 3-alkoxy- and 3-aryloxy-propane 1 : 2-epoxides with 4-ethoxycarbonyl-4-phenylpiperidine [2] (I; R = H), obtaining the compounds listed in the Table. Their biological study, for which we are indebted to Dr. A. David and Dr. C. Bianchi (B.D.H. Biological Department, Godalming, Surrey) revealed that many of them were highly potent analgesics in the tail-pinch technique in mice. Similar types (I) in which the nitrogen substituent (R) is phenethyl,[3] α-hydroxyphenethyl,[3] *p*-aminophenethyl,[4,5] 2-morpholinoethyl and 2-(1 : 2 : 3 : 6-tetrahydropyridino)ethyl [6] were reported by other groups of workers while the present work was in progress. In addition 4-phenyl-4-propionylpiperidine (I*a*; R = H), readily prepared by reaction between 4-cyano-4-phenyl-1-toluene-*p*-sulphonylpiperidine [2] and ethylmagnesium bromide, was condensed with 1 : 2-epoxy-3-phenoxypropane to give the related 1-(2-hydroxy-3-phenoxypropyl)-4-phenyl-4-propionylpiperidine [I*a*; R = Ph·O·CH_2·CH(OH)·CH_2]. Reaction between 1 : 5-dichloro-3-cyano-3-phenylpentane and 2-hydroxy-3-*o*-tolyloxypropylamine furnished the related 4-cyano-1-(2-hydroxy-3-*o*-tolyloxypropyl)-4-phenylpiperidine (hydrochloride).

Attention was next directed to the preparation of analogous derivatives of 4-hydroxy-4-phenylpiperidine [7-10] (I*b*; R = R″ = H), which were required as their 4-propionates. The parent base (I*b*; R = R″ = H), was initially obtained by a variation of the method originally described by Hartough *et al.*,[11] and more fully investigated by Schmidle and Mansfield,[12] in which α-methylstyrene is condensed with aqueous formaldehyde and ammonium chloride to yield tetrahydro-6-methyl-6-phenyl-1 : 3-oxazine (III; R = H), which passes on acid hydrolysis into the required piperidinol. For larger-scale work its preparation by direct aqueous hydrolysis of 4-bromo-4-phenylpiperidine [13] proved more convenient. Condensation of 4-hydroxy-4-phenylpiperidine (I*b*; R = R″ = H) with 1 : 2-epoxy-3-phenoxy- and 1 : 2-epoxy-3-*o*-tolyloxy-propane furnished the corresponding 4-hydroxy-1-(2-hydroxy-3-aryloxypropyl)-4-phenylpiperidine [I*b*; R″ = H, R = Ph·O·CH_2·CH(OH)·CH_2 or Me·C_6H_4·O·CH_2·CH(OH)·CH_2]. The phenoxy-diol [I*b*; R″ = H, R = Ph·O·CH_2·CH(OH)·CH_2] was also prepared in low overall yield by condensation of 2-hydroxy-3-phenoxypropylamine hydrochloride with α-methylstyrene and formaldehyde

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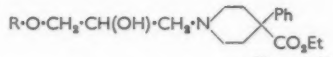


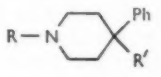
R	Base or salt *	M. p.	Formula	Found (%) C	H	N	Cl	Required (%) C	H	N	Cl
H	B	77—79° †	$C_{17}H_{25}O_4N$	66·8	8·2	4·6		66·4	8·2	4·6	
	B,HCl	151—152	$C_{17}H_{26}O_4NCl$			4·2	10·5			4·1	10·3
	B,P *	145—146	$C_{23}H_{28}O_{11}N_4$			10·2				10·4	
Et	B,HCl	141—143	$C_{19}H_{30}O_4NCl$	61·2	7·6	3·8	9·9	61·3	8·1	3·8	9·6
Bu^n	B,HCl	154	$C_{21}H_{34}O_4NCl$	63·2	8·6	3·8		63·0	8·6	3·5	
	B,P	89—91	$C_{27}H_{37}O_{11}N_4$	54·3	5·9	9·1		54·6	6·3	9·4	
Ph	B	111	$C_{23}H_{29}O_4N$	72·2	7·7	3·8		72·0	7·6	3·7	
	B,HCl	178—179 / 146—148	$C_{23}H_{30}O_4NCl$	65·6 / 65·7	7·3 / 7·3	3·2 / 3·4	8·4 / 8·5	65·8	7·2	3·3	8·5
	B,HBr	163—164	$C_{23}H_{30}O_4NBr$	59·3	6·2	2·9	17·4 (Br)	59·5	6·5	3·0	17·2 (Br)
	B,P	152	$C_{29}H_{33}O_{11}N_4$	56·7	5·4	9·4		56·8	5·3	9·2	
	B,H_2SO_4	181 / 264	$C_{23}H_{31}O_6NS$	57·7 / 57·6	6·5 / 6·6	3·1 / 3·2		57·4	6·5	2·9	
	B,H_3PO_4	174—175	$C_{23}H_{32}O_8NP$	57·3	6·8	3·0		57·4	6·7	2·9	
	B,I	131—133	$C_{25}H_{36}O_6NS$	58·7	7·0	2·9		58·9	6·9	2·8	
	B,S	166	$C_{23}H_{32}O_7N_2S$	57·7	7·1	6·0	6·8 (S)	57·5	6·7	5·8	6·7 (S)
	B,L	131—133	$C_{26}H_{35}O_7N$	66·0	7·4	2·8		65·9	7·5	3·0	
	B,G	153—154	$C_{26}H_{35}O_{10}NP$	56·3	7·1	2·4		56·2	6·9	2·5	
	B,T	137—138	$C_{60}H_{64}O_{14}N_2$	65·4	7·0	2·7		65·5	7·0	3·1	
	B,M	150—151	$C_{24}H_{33}O_7N_5$	60·5	6·9	3·0		60·1	7·0	2·9	
	B,H_3PO_2	116—118	$C_{23}H_{32}O_6NP,\frac{1}{2}H_2O$	60·5	6·8	3·1		60·2	7·2	3·1	
o-Tolyl	B	81—83	$C_{24}H_{31}O_4N$	72·3	7·7	3·4		72·5	7·9	3·5	
	B,HCl	188—189	$C_{24}H_{32}O_4NCl$	66·2	7·7	3·3	8·4	66·4	7·4	3·2	8·2
	B,P	164—166	$C_{30}H_{34}O_{11}N_4$	57·4	5·2	8·7		57·5	5·5	8·9	
m-Tolyl	B	80—81	$C_{24}H_{31}O_4N$	72·1	8·0	3·5		72·5	7·9	3·5	
	B,HCl	157—159	$C_{24}H_{32}O_4NCl$	66·1	7·1	3·0	8·4	66·4	7·4	3·2	8·2
	B,P	151—152	$C_{30}H_{34}O_{11}N_4$	57·5	5·4	9·0		57·5	5·5	8·9	
	B,G	139—145	$C_{27}H_{40}O_{10}NP$	56·7	6·9	2·5		56·9	7·1	2·5	
p-Tolyl	B	111—113	$C_{24}H_{31}O_4N$	73·1	7·9	3·4		72·5	7·9	3·5	
	B,HCl	152—154	$C_{24}H_{32}O_4NCl$	65·8	7·3	3·0	8·4	66·4	7·4	3·2	8·2
	B,P	168—169	$C_{30}H_{34}O_{11}N_4$	57·2	5·2	8·8		57·5	5·5	8·9	
o-C_6H_4·OMe	B	89—90	$C_{24}H_{31}O_5N$	70·2	7·8	3·7		69·7	7·6	3·4	
	B,HCl	147—148	$C_{24}H_{32}O_5NCl$	63·6	7·1	3·3	7·7	64·0	7·2	3·1	7·9
	B,P	159—160	$C_{30}H_{34}O_{12}N_4$			8·4				8·7	
o-C_6H_4F	B	80—81	$C_{23}H_{28}O_4NF$	68·5	7·1			68·8	7·0		
	B,HCl	158—159	$C_{23}H_{29}O_4NClF$	63·2	7·0	3·4	8·5	63·1	6·7	3·2	8·1
	B,P	132—134	$C_{29}H_{31}O_{11}N_4F$			9·1				8·9	
o-C_6H_4Cl	B	81—83	$C_{23}H_{28}O_4NCl$	66·6	6·8	3·5	8·4	66·1	6·8	3·4	8·5
	B,HCl	171—172	$C_{23}H_{29}O_4NCl_2$	61·3	6·5	3·1		60·8	6·4	3·1	
	B,P	153—155	$C_{29}H_{31}O_{11}N_4Cl$	53·9	4·7	8·7	5·2	53·8	4·8	8·7	5·5
m-C_6H_4Cl	B	89—90	$C_{23}H_{28}O_4NCl$	66·2	6·7	3·4	8·6	66·1	6·8	3·4	8·5
	B,HCl	162—163	$C_{23}H_{29}O_4NCl_2$	60·6	6·4	3·1	15·5	60·8	6·4	3·1	15·6
	B,P	139—140	$C_{29}H_{31}O_{11}N_4Cl$	53·6	4·8	8·6	5·4	53·8	4·8	8·7	5·5
	B,G	129—133	$C_{26}H_{37}O_{10}NClP$	53·0	6·4	2·2	6·3	52·9	6·3	2·4	6·0
p-C_6H_4Cl	B	103—104	$C_{23}H_{28}O_4NCl$	66·1	6·5	3·7	8·7	66·1	6·8	3·4	8·5
	B,HCl	165—166	$C_{23}H_{29}O_4NCl_2$	60·6	6·3	3·3	15·8	60·8	6·4	3·1	15·6
	B,P	148	$C_{29}H_{31}O_{11}N_4Cl$			8·7	5·5			8·7	5·5
	B,G	135—138	$C_{26}H_{37}O_{10}NClP$	52·1	6·2	2·6	6·2	52·9	6·3	2·4	6·0
o-C_6H_4·C_3H_5	B,HCl	204—206(d)	$C_{26}H_{34}O_4NCl$	67·9	7·4	3·1	7·6	67·9	7·5	3·0	7·7
	B,P	139—140	$C_{32}H_{36}O_{11}N_4$	58·8	5·4			58·9	5·6		
	B,G	125—127	$C_{29}H_{42}O_{10}NP$	58·6	7·1	2·3		58·5	7·1	2·4	
p-C_6H_4·NHAc	B	144—145	$C_{25}H_{32}O_5N_2$	68·6	7·6	6·2		68·1	7·3	6·4	
p-C_6H_4·NH_2	B,HCl	*ca.* 230(d)	$C_{23}H_{32}O_4N_2Cl_2,\frac{1}{2}H_2O$	57·4	6·8	5·7		57·5	6·9	5·8	
p-C_6H_4·CO_2Et	B	86—88	$C_{26}H_{33}O_6N$	68·7	7·0	2·7		68·5	7·3	3·1	
	B,HCl	176—178	$C_{26}H_{34}O_6NCl$	63·2	7·1	2·9	7·3	63·4	7·0	2·8	7·2
	B,P	160—161	$C_{32}H_{36}O_{13}N_4$	56·3	5·3	7·9		56·1	5·3	8·2	
$CHPh_2$	B,HCl	171—172	$C_{30}H_{36}O_4NCl$	70·6	7·0	2·9	7·1	70·1	7·1	2·7	7·0
	B,P	128—130	$C_{36}H_{38}O_{11}N_4$	61·6	5·6	8·4		61·5	5·5	8·0	
*cyclo*Hexyl	B,HCl	164—166	$C_{22}H_{36}O_4NCl$	64·9	8·7	3·3	8·2	64·8	8·5	3·3	8·3
RO: Δ²-Piperidino	B,HCl	181—185(d)	$C_{25}H_{34}O_3N_2Cl_2,H_2O$	57·1	7·3	6·0	15·6	57·0	7·8	6·0	15·3
RO: Δ²-Piperidino	B,P	182—183	$C_{34}H_{38}O_{17}N_8,H_2O$	48·1	4·4	13·1		48·1	4·7	13·2	
RO: Morpholino	B	70—72	$C_{21}H_{32}O_4N_2$	67·1	8·5	7·7		67·0	8·6	7·4	
RO: Morpholino	B,HCl	206	$C_{21}H_{34}O_4NCl_2,\frac{1}{2}H_2O$	55·0	7·8	6·0		55·0	7·7	6·1	
RO: Morpholino	B,P	181—182	$C_{33}H_{38}O_{16}N_8$	47·3	4·5	13·2		47·5	4·6	13·4	

* B = Base; B,P = Picrate; B,G = α-Glycerophosphate; B,I = Isethionate; B,S = Sulphamate; B,L = Lactate; B,T = Tartrate; B,M = Methanesulphonate. † B. p. 194°/0·3 mm.

XUM

to yield tetrahydro-3-(2-hydroxy-3-phenoxypropyl)-6-methyl-6-phenyl-1 : 3-oxazine [III; R = $Ph{\cdot}O{\cdot}CH_2{\cdot}CH(OH){\cdot}CH_2$], followed by hot acid hydrolysis.

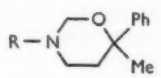
Acylation of the foregoing diols with propionic anhydride–concentrated sulphuric acid furnished the dipropionates. Their selective hydrolysis to the 4-monopropionates, however, could not be achieved; *e.g.*, treatment with 1 equiv. of ethanolic sodium hydroxide



(I ; R′ = CO_2Et)
(I*a* ; R′ = COEt)
(I*b* ; R′ = OR″)

$Ar{\cdot}O{\cdot}CH_2{\cdot}CH(OH){\cdot}CH_2{\cdot}$

(II)



(III)

at room temperature or with 1 equiv. of anhydrous sodium carbonate in methanol under reflux furnished only the respective diols.

In view of these discouraging results we turned to the preparation of 4-phenyl-4-propionoxypiperidine (I*b*; R = H, R″ = COEt), intending to condense this intermediate with the appropriate 3-aryloxy-1 : 2-epoxypropane.

Treatment of the hydrochloride (from I*b*; R = R″ = H) with acetic or propionic anhydride at 100° led to recovery of unchanged material. Enforced acylation in the presence of a trace of concentrated sulphuric acid resulted in the formation of 1-acetyl- and 1-propionyl-1 : 2 : 3 : 6-tetrahydro-4-phenylpyridine, respectively.

Debenzylation of 1-benzyl-4-phenyl-4-propionoxypiperidine (I*b*; R = CH_2Ph, R″ = COEt) was next examined. Catalytic hydrogenation with 1 mol. of hydrogen furnished unchanged material (32%), 4-phenylpiperidine (38%), and smaller amounts of 1-benzyl-4-phenylpiperidine, 4-hydroxy-4-phenyl-1-propionylpiperidine, and the propionic acid salt of 4-hydroxy-4-phenylpiperidine. The facile loss of the propionate group during catalytic hydrogenation was unexpected, but probably arises from the relation between the 4-hydroxyl and 4-phenyl groups of (I*b*; R″ = H) which constituted a substituted benzyl alcohol. In support thereof we find that catalytic hydrogenation of 1-benzyl-4-hydroxy-4-phenylpiperidine (I*b*; R = CH_2Ph, R″ = H) gives the expected 4-hydroxy-4-phenylpiperidine as sole identifiable product. In the expectation that the diphenylmethyl group would be removed more readily than benzyl, the condensation of 4-hydroxy-4-phenylpiperidine with diphenylmethyl bromide was examined, but only 1-diphenylmethyl-1 : 2 : 3 : 6-tetrahydro-4-phenylpyridine was obtained. No better results attended attempts to convert 4-bromo-4-phenylpiperidine into the 4-propionoxy-derivative with sodium propionate, dehydrohalogenation with concomitant *N*-acylation taking place with formation of 4-hydroxy-4-phenyl-1-propionylpiperidine. Production of the last compound presumably involves the formation of a 4-propionoxy-intermediate followed by $O \longrightarrow N$ migration of the acyl residue.

In a further approach to the required 4-monopropionates, 2-diphenylmethoxy-3-phenoxypropyl chloride and bromide were prepared by reaction of the 2-hydroxy-3-phenoxypropyl halides with diphenylmethanol in the presence of toluene-*p*-sulphonic acid as catalyst.[14] Their condensation with 4-hydroxy-4-phenylpiperidine yielded the required intermediate [I*b*; R = $Ph{\cdot}O{\cdot}CH_2{\cdot}CH(O{\cdot}CHPh_2){\cdot}CH_2$, R″ = H] which resisted propionylation, however, presumably through steric hindrance introduced by the diphenylmethyl residue. The tetrahydropyranyl ether of 2-hydroxy-3-phenoxypropyl chloride was cleaved during condensation with the piperidinol. Reaction of 3-phenoxy-2-propionoxypropyl chloride with 2 mols. of the piperidinol in 2-ethoxyethanol gave the propionyl derivative (I*b*; R = COEt, R″ = H) and the base [I*b*; R = $Ph{\cdot}O{\cdot}CH_2{\cdot}CH(OH){\cdot}CH_2$, R″ = H].

[14] Petrow, Stephenson, and Thomas, *J. Pharm. Pharmacol.*, 1956, **8**, 666.

XUM

Experimental

M. p.s are uncorrected.

The methods employed for the preparation of the compounds listed in the Table are illustrated by the following four examples.

1-(2 : 3-*Epoxypropyl*)-1 : 2 : 3 : 6-*tetrahydropyridine*.—2 : 3-Epoxypropyl chloride (92·5 g.) was added slowly with stirring at <30° to 1 : 2 : 3 : 6-tetrahydropyridine (83 g.) in water (400 ml.). After being stirred at 25—30° for 4 hr. the mixture was cooled to 0° and treated slowly with sodium hydroxide (42 g.) in water (60 ml.); it was then saturated with salt and extracted with chloroform. After removal of the chloroform the residual oil was distilled under reduced pressure to yield the *product*, b. p. 34°/0·3 mm. (Found: C, 68·8; H, 9·5; N, 9·7. $C_8H_{13}ON$ requires C, 69·0; H, 9·4; N, 10·1%).

4-*Ethoxycarbonyl*-1-[2-*hydroxy*-3-(1 : 2 : 3 : 6-*tetrahydropyridino*)*propyl*]-4-*phenylpiperidine Dihydrochloride Hydrate*.—The foregoing epoxide (5·8 g.) and 4-ethoxycarbonyl-4-phenylpiperidine (9·35 g.) in light petroleum (20 ml., b. p. 60—80°) were heated under reflux for 2 hr. After removal of the solvent the residual base was converted in ethanol–ether into the *dihydrochloride* which crystallised from the same solvent in needles.

4-*Ethoxycarbonyl*-4-*phenyl*-1-(3-cyclo*hexyloxy*-2-*hydroxypropyl*)*piperidine Hydrochloride*.—A solution of 3-*cyclo*hexyloxy-2-hydroxypropyl chloride (9·65 g.) and 4-ethoxycarbonyl-4-phenylpiperidine (11·7 g.) in ethanol (25 ml.) was treated with anhydrous sodium carbonate (3 g.), and the mixture heated under reflux for 10 hr. The base, isolated by dilution with water and extraction with chloroform, was converted directly into the *hydrochloride* which separated from ethanol–ether in prisms.

4-*Ethoxycarbonyl*-1-(2-*hydroxy*-3-m-*tolyloxypropyl*)-4-*phenylpiperidine*.—A solution of 1 : 2-epoxy-3-*m*-tolyloxypropane (8·2 g.) and 4-ethoxycarbonyl-4-phenylpiperidine (11·7 g.) in light petroleum (15 ml., b. p. 60—80°) was heated under reflux for 1 hr. The *product* separated in fluffy needles on cooling and was crystallised from aqueous ethanol. The *hydrochloride* separated from ethanol–ether in minute needles.

1-(2-*Acetoxy*-3-*phenoxypropyl*)-4-*ethoxycarbonyl*-4-*phenylpiperidine hydrochloride*, m. p. 143° after crystallisation from benzene (Found: C, 65·6; H, 6·9; N, 2·9; Cl, 8·0. $C_{25}H_{32}O_5NCl$ requires C, 65·0; H, 7·0; N, 3·0; Cl, 7·7%), was obtained by reaction of 4-ethoxycarbonyl-1-(2-hydroxy-3-phenoxypropyl)-4-phenylpiperidine (8 g.) with acetyl chloride (1·8 g.) in benzene (40 ml.) under reflux for 1½ hr.

1-(2-*Benzoyloxy*-3-*phenoxypropyl*)-4-*ethoxycarbonyl*-4-*phenylpiperidine hydrochloride* had m. p. 172—176° (Found: C, 68·3; H, 7·0; N, 2·7; Cl, 6·6. $C_{30}H_{34}O_5NCl$ requires C, 68·7; H, 6·6; N, 2·7; Cl, 6·8%) after crystallisation from ethanol–ether. The *base*, m. p. 86—88° (Found: N, 3·1. $C_{30}H_{33}O_5N$ requires N, 2·9%), crystallised from light petroleum (b. p. 60—80°).

4-*Ethoxycarbonyl*-1-(2-*hydroxy*-3-*phenoxypropyl*)-4-*phenylpiperidine* N-*oxide hydrochloride*, m. p. 170° (decomp.) (Found: C, 63·4; H, 6·9; N, 3·5. $C_{23}H_{30}O_5NCl$ requires C, 63·3; H, 7·0; N, 3·2%) after crystallisation from ethanol–ether, was prepared by the action of peracetic acid solution on the base at 80° for 1 hr.

4-*Ethoxycarbonyl*-1-(2-*hydroxy*-2-*methyl*-3-*phenoxypropyl*)-4-*phenylpiperidine hydrochloride*, needles, m. p. 171—172° (Found: C, 66·7; H, 7·3; N, 3·4; Cl, 8·3. $C_{24}H_{32}O_4NCl$ requires C, 66·4; H, 7·4; N, 3·2; Cl, 8·2%) after crystallisation from ethanol, was prepared by condensation of 1 : 2-epoxy-2-methyl-3-phenoxypropane (8·2 g.) with 4-ethoxycarbonyl-4-phenylpiperidine (11·65 g.) in light petroleum (25 ml., b. p. 60—80°) under reflux for 2 hr., followed by treatment of the product with hydrogen chloride. The *picrate* had m. p. 109—111° (Found: C, 57·4; H, 5·7; N, 8·6. $C_{30}H_{34}O_{11}N_4$ requires C, 57·5; H, 5·5; N, 8·9%) after crystallisation from ethyl acetate–light petroleum (b. p. 60—80°).

4-*Ethoxycarbonyl*-1-(2-*hydroxy*-2-*methyl*-3-o-*tolyloxypropyl*)-4-*phenylpiperidine hydrochloride* separated from ethyl acetate in needles, m. p. 177° (Found: C, 66·8; H, 8·0; N, 3·2; Cl, 7·9. $C_{25}H_{34}O_4NCl$ requires C, 67·0; H, 7·7; N, 3·1; Cl, 7·9%). The *picrate* had m. p. 130—131° (Found: C, 58·0; H, 5·6; N, 9·2. $C_{31}H_{36}O_{11}N_4$ requires C, 58·1; H, 5·7; N, 8·8%) after crystallisation from ethyl acetate–light petroleum (b. p. 40—60°).

4-*Phenyl*-4-*propionyl*-1-*toluene*-p-*sulphonylpiperidine*.—To a stirred solution of ethylmagnesium bromide [prepared from magnesium (3 g.) and ethyl bromide (15 g.) in ether (20 ml.) and anisole (20 ml.)] a solution of 4-cyano-4-phenyl-1-toluene-*p*-sulphonylpiperidine (16 g.) in

anisole (90 ml.) was added slowly, and reaction completed by heating on the steam-bath for 2 hr. After cooling in ice, water was added, the mixture was acidified with hydrochloric acid, and the solvents were removed by steam distillation. The residual product, after drying at 60°, had m. p. 84—89° (yield 86%). Its purification proved difficult and the material was directly hydrolysed as indicated below.

4-*Phenyl*-4-*propionylpiperidine Hydrochloride*.—The foregoing compound (44 g.) was heated under reflux for 2 hr. with concentrated sulphuric acid (70 ml.) and water (40 ml.). The mixture was diluted with water and extracted with benzene to remove non-basic material. The aqueous phase was made alkaline with aqueous sodium hydroxide, and the product isolated with benzene, and converted into the *hydrochloride* (32 g.), m. p. 210° (Found: C, 66·4; H, 7·8; N, 5·5; Cl, 14·0. $C_{14}H_{20}ONCl$ requires C, 66·2; H, 7·9; N, 5·5; Cl, 14·0%) after crystallisation from ethanol–ether.

1-(2-*Hydroxy*-3-*phenoxypropyl*)-4-*phenyl*-4-*propionylpiperidine Hydrochloride*.—The foregoing hydrochloride (10 g.) was converted into the base, which was treated in benzene (20 ml.) with 1 : 2-epoxy-3-phenoxypropane (8 g.). The mixture was heated on the steam-bath for 3 hr., cooled, and treated with a slight excess of hydrogen chloride. The *hydrochloride* had m. p. 187° (Found: C, 68·3; H, 7·1; N, 3·5; Cl, 8·8. $C_{23}H_{30}O_3NCl$ requires C, 68·4; H, 7·5; N, 3·5; Cl, 8·8%) after crystallisation from ethanol–ether.

4-*Cyano*-1-(2-*hydroxy*-3-*o*-*tolyloxypropyl*)-4-*phenylpiperidine Hydrochloride*.—A mixture of 1 : 5-dichloro-3-cyano-3-phenylpentane (5 g.) and 2-hydroxy-3-*o*-tolyloxypropylamine (10 g.) in hexanol (100 ml.) was heated under reflux for 2 hr., the solvent removed by steam-distillation, and the residue acidified with concentrated hydrochloric acid. The *product* which separated had m. p. 226° (Found: C, 68·2; H, 7·3; N, 7·1; Cl, 9·1. $C_{22}H_{27}O_2N_2Cl$ requires C, 68·3; H, 7·0; N, 7·2; Cl, 9·2%) after crystallisation from ethanol–ether.

4-*Hydroxy*-4-*phenylpiperidine*.[12]—(*a*) The following improved procedure was adopted: A solution of tetrahydro-6-methyl-6-phenyl-1 : 3-oxazine (147 g.) in 18·5% hydrochloric acid (177 g.) was heated on the steam-bath for 30 min. and set aside overnight. Heating was continued for 2½ hr., and the mixture again left overnight. It was then poured into water (580 ml.) and made alkaline with excess of 50% sodium hydroxide solution, and the separated oil isolated with toluene. After concentration of the toluene extract, the product (37 g.) separated on cooling and was collected. Concentration of the filtrate followed by distillation of the residue at 0·2 mm. yielded 62 g. of unchanged material (b. p. 120°) and a higher-boiling fraction which yielded a further 6·3 g. of the piperidinol. Crystallisation of the combined crops from toluene yielded the product (37·35 g.), m. p. 158—160°.

(*b*) 1 : 2 : 3 : 6-Tetrahydro-4-phenylpyridine (50 g.) was added dropwise with stirring to 50% w/v hydrobromic acid in acetic acid (150 ml.), below 25°. The paste was diluted with acetic acid (100 ml.), and stirring continued for 30 min. The solid 4-*bromo*-4-*phenylpiperidine* hydrobromide (84 g.) was collected, washed with a little acetic acid and with ether and crystallised from ethanol–ether, forming fawn needles, m. p. 209—211° (Found: C, 40·9; H, 4·8; N, 4·4; Br, 49·5. $C_{11}H_{15}NBr_2$ requires C, 41·1; H, 4·7; N, 4·4; Br, 49·8%).

The foregoing hydrobromide (3·21 g.) in water (40 ml.) was heated on the steam-bath for 1 hr., and the solution made alkaline with 50% sodium hydroxide solution to yield 4-hydroxy-4-phenylpiperidine (90%), m. p. 158—160°. The hydrochloride crystallised from ethanol–ether in needles, m. p. 223—224° (decomp.). The *oxalate* separated from ethanol in cubes, m. p. 202—203° (decomp.) (Found: C, 58·7; H, 6·5. $C_{13}H_{17}O_5N$ requires C, 58·5; H, 6·4%).

4-*Hydroxy*-1-(2-*hydroxy*-3-*phenoxypropyl*)-4-*phenylpiperidine*.—(*a*) A solution of 4-hydroxy-4-phenylpiperidine (10·62 g.) in acetone (100 ml.) was treated with 1 : 2-epoxy-3-phenoxypropane (9·0 g.), and the solution heated on the steam-bath for 2 hr. After removal of solvent, the residual solid was crystallised from ethanol to yield the *product* (18·5 g.) in prisms, m. p. 120—122°, b. p. 232°/0·5 mm. (Found: C, 73·6; H, 7·6; N, 4·1. $C_{20}H_{25}O_3N$ requires C, 73·4; H, 7·7; N, 4·3%). The *hydrochloride* had m. p. 138—140° (Found: C, 66·2; H, 7·4; N, 3·4; Cl, 10·2. $C_{20}H_{26}O_3NCl$ requires C, 66·0; H, 7·2; N, 3·4; Cl, 9·8%) after crystallisation from ethanol–ether.

(*b*) A mixture of 2-hydroxy-3-phenoxypropylamine hydrochloride (38·0 g., 0·187 mole) and α-methylstyrene (22 g., 0·187 mole) was heated to 60° with vigorous stirring, 37% formaldehyde solution (63·6 g., 0·783 mole) added, and the mixture heated at 85° for 5 hr. It was then cooled, made alkaline with excess of 50% aqueous sodium hydroxide, and the oil isolated with toluene, and distilled at 0·2 mm. to yield a fraction (24 g.), b. p. 196—230°. This was dissolved in dry

ether and slowly deposited 4-hydroxy-1-(2-hydroxy-3-phenoxypropyl)-4-phenylpiperidine (3·2 g.), m. p. 120—121°, which was removed. The fraction soluble in ether was distilled at 0·5 mm. to yield tetrahydro-3-(2-hydroxy-3-phenoxypropyl)-6-methyl-6-phenyl-1 : 3-oxazine, b. p. 210—220°. It formed a *hydrochloride*, m. p. 156—157° (Found: C, 65·9; H, 7·2. $C_{21}H_{25}O_3NCl$ requires C, 66·0; H, 7·2%) strongly depressed on admixture with the hydrochloride of the foregoing piperidinol (m. p. 138—140°).

The oxazine base (5·5 g., 0·0168 mole) was dissolved in 18·5% hydrochloric acid (3·6 g., 0·0168 mole), and the solution heated on the steam-bath for 7 hr. It was stored at room temperature for 3 days, reheated for 3 hr., then cooled and made alkaline with excess of 50% aqueous sodium hydroxide. The oil which separated was isolated with ether and distilled at 0·25 mm. Unchanged oxazine (2·8 g., 51%) was obtained, b. p. 204—212°, together with 4-hydroxy-1-(2-hydroxy-3-phenoxypropyl)-4-phenylpiperidine (1·5 g., 27%), b. p. 227—231°, m. p. 118—120° after crystallisation from ethanol.

1-(3-*Phenoxy*-2-*propionoxypropyl*)-4-*phenyl*-4-*propionoxypiperidine*.—The foregoing *diol* (10 g.), dissolved in propionic anhydride (100 ml.), was treated with concentrated sulphuric acid (4 drops), and the mixture heated on the steam-bath for 3 hr. After removal of propionic anhydride at reduced pressure, the residue was partitioned between ether and aqueous sodium carbonate. The dried ethereal extract was treated with a slight excess of hydrogen chloride. The resultant *hydrochloride* separated from acetone in shining plates, m. p. 129—131° (Found: C, 65·4; H, 7·2; N, 3·3. $C_{26}H_{34}O_5NCl$ requires C, 65·6; H, 7·2; N, 2·9%).

4-*Hydroxy*-1-(2-*hydroxy*-3-*o*-*tolyloxypropyl*)-4-*phenylpiperidine* separated from aqueous ethanol in prisms, m. p. 131° (Found: C, 73·6; H, 7·8; N, 4·2. $C_{21}H_{27}O_3N$ requires C, 73·9; H, 7·9; N, 4·1%). The *hydrochloride* crystallised from ethanol–ether in small plates, m. p. 175—177° (Found: N, 3·8; Cl, 9·4. $C_{21}H_{28}O_3NCl$ requires N, 3·7; Cl, 9·4%).

The *dipropionate hydrochloride* formed small plates, m. p. 175—176° (Found: C, 65·7; H, 7·6; N, 2·8; Cl, 7·0. $C_{27}H_{36}O_5NCl$ requires C, 66·2; H, 7·4; N, 2·9; Cl, 7·2%), from acetone. It (2 g., 0·004 mole) was converted into the base, which was dissolved in methanol (10 ml.), anhydrous sodium carbonate (0·2 g., 0·002 mole) added, and the mixture heated under reflux for 3 hr. and filtered, the filtrate evaporated to dryness, and the residue crystallised from ethanol to yield the original diol (0·5 g.), m. p. 130—132°.

1-*Benzyl*-4-*hydroxy*-4-*phenylpiperidine* (cf. [10,12]).—To a solution of 4-hydroxy-4-phenylpiperidine (17·7 g.) in *tert.*-butyl alcohol (100 ml.) was added a solution of sodium *tert.*-butoxide [from sodium (2·3 g.) in *tert.*-butyl alcohol (100 ml.)], followed by benzyl chloride (12·95 g.), and the mixture heated under reflux for 1 hr. It was diluted with methanol and filtered, the filtrate evaporated to dryness under reduced pressure, and the residue crystallised from light petroleum (b. p. 60—80°). The product (22·5 g., 82%) had m. p. 107—109°, b. p. 176°/0·1 mm. Its hydrochloride formed needles, m. p. 224—225° (Found: C, 71·2; H, 7·4; N, 4·6; Cl, 11·6. Calc. for $C_{18}H_{22}ONCl$: C, 71·2; H, 7·3; N, 4·6; Cl, 11·7%), from ethanol–ether.

1-Benzyl-4-phenyl-4-propionoxypiperidine hydrochloride,[10] m. p. 189—190° (Found: C, 70·3; H, 7·2; N, 4·1; Cl, 10·1. Calc. for $C_{21}H_{26}O_2NCl$: C, 70·1; H, 7·2; N, 3·9; Cl, 9·8%) after crystallisation from ethanol–ether, was prepared by treatment of the foregoing base (9 g.) with propionic anhydride (90 ml.) containing concentrated sulphuric acid (7 drops) on the steam-bath for 6 hr. The *base* had b. p. 174—177°/0·4 mm.

Hydrogenation of 1-*Benzyl*-4-*phenyl*-4-*propionoxypiperidine*.—(*a*) A solution of the base (22 g.) in ethanol (200 ml.) was hydrogenated at room temperature by using 5% palladium–charcoal catalyst (5 g.), and the reaction stopped when 1 mol. of hydrogen had been absorbed. The product was distilled at 0·5 mm. A small quantity (*ca.* 0·4 g.) of propionic acid was collected, followed by fractions: (i) 4·2 g., b. p. 94—102°; (ii) 2·3 g., b. p. 120—150°; (iii) 4·2 g., b. p. 150—170°; and (iv) 7·15 g., b. p. 170—182°. Fraction (i) solidified on cooling and proved to be 4-phenylpiperidine.[15] It formed a *picrate*, m. p. 162—163° (Found: N, 14·6. $C_{17}H_{18}O_7N_4$ requires N, 14·4%) from ethanol. An authentic specimen of 4-phenylpiperidine, prepared by hydrogenation of 1 : 2 : 3 : 6-tetrahydro-4-phenylpyridine in ethanol with palladised charcoal at room temperature, had b. p. 133—135°/11 mm., m. p. 57—58°, and formed a picrate, m. p. 161—163°, identical with that described above. Fractions (ii) and (iii) were combined and on trituration with ether yielded 4-*hydroxy*-4-*phenylpiperidine propionate* (1·5 g.), m. p. 163—165° (Found: C, 66·9; H, 8·5; N, 5·5. $C_{14}H_{21}O_3N$ requires C, 66·9; H, 8·4; N, 5·6%) after crystallisation from ethyl acetate, identical with synthetic material. After removal of this salt

[15] Adkins, Kuick, Farlow, and Wojcik, *J. Amer. Chem. Soc.*, 1934, **56**, 2427.

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the residual oil was distilled at 0·4 mm. to yield 1-benzyl-4-phenylpiperidine [16] (1·9 g.), b. p. 151°, n_D^{22} 1·5692, which formed a *picrate*, m. p. 151—152° (Found: C, 60·1; H, 5·0; N, 11·7. $C_{24}H_{24}O_7N_4$ requires C, 60·0; H, 5·0; N, 11·7%). The m. p. was not depressed on admixture with an authentic sample. Fraction (iv), on treatment with ether, yielded 4-*hydroxy-4-phenyl-1-propionylpiperidine* (1·6 g.), which separated from ethyl acetate in prisms, m. p. 173—174° (Found: C, 71·6; H, 7·7; N, 6·2. $C_{14}H_{19}O_2N$ requires C, 72·1; H, 8·2; N, 6·0%). An authentic sample was prepared for comparison by heating the propionate of 4-hydroxy-4-phenylpiperidine for 20 min. at 240—250° and crystallising the residue from ethyl acetate.

(*b*) The foregoing hydrogenation was repeated, but after removal of the catalyst and the alcohol, the residue was extracted with ether and the extract washed with aqueous sodium carbonate to remove free propionic acid. The dried ethereal extract deposited 4-hydroxy-4-phenylpiperidine (50·5%), m. p. 158—160°, on cooling. Concentration of the filtrate followed by distillation of the residual oil at 1·2 mm. yielded 4-phenylpiperidine (9%), b. p. 98—100°, together with starting material (29%), b. p. 188—192°.

Hydrogenation of 1-*Benzyl-4-hydroxy-4-phenylpiperidine.*—A solution of this piperidine (16 g.) in ethanol (150 ml.) was hydrogenated at 60° by using 5% palladium–charcoal (5 g.). The slow reaction was stopped when 0·95 mol. of hydrogen had been absorbed. After removal of catalyst and solvent, the residue crystallised from toluene to yield prisms of 4-hydroxy-4-phenylpiperidine (8 g.), m. p. 158—160°.

1 : 2 : 3 : 6-*Tetrahydro-4-phenyl-1-propionylpyridine.*—To a solution of 4-hydroxy-4-phenylpiperidine hydrochloride (10·65 g.) in propionic anhydride (200 ml.) was added concentrated sulphuric acid (10 drops), and the mixture heated on the steam-bath for 1 hr. After removal of the anhydride under reduced pressure the residue was made alkaline with aqueous sodium carbonate, and the oil isolated with ether and purified by distillation at 0·3 mm. to yield the *product*, b. p. 158—160° (Found: C, 77·7; H, 8·0; N, 6·7. $C_{14}H_{17}ON$ requires C, 78·1; H, 7·9; N, 6·5%). A corresponding reaction with acetic anhydride gave a 93% yield of the acetyl analogue, b. p. 163—165°/0·5 mm., m. p. 67—69°, not depressed on admixture with an authentic specimen.

1-*Diphenylmethyl*-1 : 2 : 3 : 6-*tetrahydro-4-phenylpyridine.*—A mixture of 4-hydroxy-4-phenylpiperidine (26·4 g., 2 mol.) and diphenylmethyl chloride (15·15 g.) was heated at 145° for 15 min. The cooled melt was extracted with boiling ethyl acetate to remove insoluble 4-hydroxy-4-phenylpiperidine hydrochloride (15·1 g.). The filtrate was evaporated to dryness, and the solid residue crystallised from ethanol to yield the *product* (17·8 g.) in needles, m. p. 128—131° (Found: C, 89·0; H, 7·2; N, 3·8. $C_{24}H_{23}N$ requires C, 88·6; H, 7·1; N, 4·3%).

Reaction of 4-*Bromo-4-phenylpiperidine Hydrobromide with Sodium Propionate in Propionic Acid.*—The foregoing hydrobromide (32·1 g.) was added to a solution of sodium propionate (19·2 g., 2 mol.) in propionic acid (200 ml.), and the mixture heated on the steam-bath with stirring for 1 hr. After removal of sodium bromide the filtrate was evaporated to dryness under reduced pressure, the residue made alkaline with dilute sodium hydroxide, and the oil isolated with ether. Distillation under reduced pressure yielded 1 : 2 : 3 : 6-tetrahydro-4-phenylpyridine (12·2 g., 77%), b. p. 100°/0·7 mm., and 4-hydroxy-4-phenyl-1-propionylpiperidine (2 g.), b. p. 194—196°/0·3 mm., m. p. 173—174° (see above).

1 : 2 : 3 : 6-*Tetrahydro*-1-(2-*hydroxy*-3-*o-tolyloxypropyl*)-4-*phenylpyridine.*—(*a*) A solution of 1 : 2 : 3 : 6-tetrahydro-4-phenylpyridine (6·36 g.) in benzene (15 ml.) was treated with 1 : 2-epoxy-3-*o*-tolyloxypropane (6·56 g.), and the mixture heated under reflux for 2 hr. Removal of the solvent followed by distillation at 0·2 mm. yielded the *product* (11·05 g.), b. p. 216—222°, m. p. 82—84° (Found: C, 77·6; H, 7·8; N, 4·6. $C_{21}H_{25}O_2N$ requires C, 78·0; H, 7·7; N, 4·3%) after crystallisation from light petroleum (b. p. 80—100°). The *hydrochloride* formed needles, m. p. 148—151° (Found: N, 3·9; Cl, 9·9. $C_{21}H_{26}O_2NCl$ requires N, 4·3; Cl, 10·2%) after crystallisation from methanol–ethyl acetate.

(*b*) A mixture of 2-hydroxy-3-*o*-tolyloxypropylamine hydrochloride (87·9 g., 0·4 mole) and 40% formaldehyde solution (66·8 g., 0·83 mole) was treated at 65° with stirring with α-methylstyrene (23·6 g., 0·2 mole) added during 10 min. The temperature was allowed to fall slowly to 30°, and methanol (50 ml.) was then added, and the mixture set aside at room temperature for 2 days. After removal of solvent under reduced pressure, concentrated hydrochloric acid (56 ml.) was added, and the mixture heated with stirring on the steam-bath for 3 hr. It was cooled, diluted with water (80 ml.), and extracted with toluene to remove non-basic material.

[16] Paden and Adkins, *J. Amer. Chem. Soc.*, 1936, **58**, 2487.

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The aqueous fraction was made alkaline with excess of 50% aqueous sodium hydroxide, and the oil isolated with three portions of toluene, and distilled at 0·25 mm. to yield the product (21·7 g.), b. p. 212—218°. The hydrochloride had m. p. 148—151° (after crystallisation from methanol–ethyl acetate), not depressed on admixture with the compound prepared as in (*a*).

The foregoing base (3·23 g.) in acetic acid (3 ml.) was treated with 50% w/v hydrobromic acid in acetic acid (3·24 ml., 2 mol.) at room temperature for 2 days. The product which separated, m. p. 176—178° (after crystallisation from ethanol–ether), proved to be the hydrobromide of the starting material.

2-*Diphenylmethoxy*-3-*phenoxypropyl Chloride*.—To a solution of diphenylmethanol (20 g., 0·108 mole) and 2-hydroxy-3-phenoxypropyl chloride (25 g., 0·134 mole) in toluene (100 ml.) was added toluene-*p*-sulphonic acid (200 mg.), and the mixture was heated in a Dean–Stark apparatus for 15 min., the calculated amount of water (1·94 ml.) then having collected. The cooled solution was washed with sodium carbonate solution and with water, the solvent removed under reduced pressure, and the residual oil distilled at 0·05 mm. to yield the *product* as a viscous oil, b. p. 178° (Found: C, 75·2; H, 6·4; Cl, 9·8. $C_{22}H_{21}O_2Cl$ requires C, 74·9; H, 6·0; Cl, 10·1%). 2-Diphenylmethoxy-3-phenoxypropyl bromide, similarly prepared, had b. p. 190°/0·05 mm.

1-(2-*Diphenylmethoxy*-3-*phenoxypropyl*)-1 : 2 : 3 : 6-*tetrahydro*-4-*phenylpyridine*.—(*a*) A mixture of 2-diphenylmethoxy-3-phenoxypropyl chloride (35·25 g., 0·1 mole) and 4-hydroxy-4-phenylpiperidine (35·4 g., 0·2 mole) was heated at 160° for 1 hr. then cooled and boiled with ethyl acetate to remove 4-hydroxy-4-phenylpiperidinium chloride (18·5 g.). The ethyl acetate extract was washed with water and dried (K_2CO_3), and the solvent removed. The residual oil was fractionated at 0·1 mm. to yield the product (65%) as an oil, b. p. 280°. The *hydrochloride* separated from ethanol–ether in needles, m. p. 186—187° (Found: C, 74·9; H, 6·8; N, 2·6; Cl, 6·8. $C_{33}H_{36}O_2NCl$ requires C, 74·8; H, 6·8; N, 2·6; Cl, 6·7%).

(*b*) A mixture of 2-diphenylmethoxy-3-phenoxypropyl chloride (14·1 g., 0·04 mole), 4-hydroxy-4-phenylpiperidine (7·08 g., 0·04 mole), and sodium *tert.*-butoxide (0·04 mole) in *tert.*-butyl alcohol (60 ml.) was heated on the steam-bath for 30 hr. Sodium chloride (0·75 g.) was removed (theory, 2·35 g.). The filtrate was concentrated, and the residue triturated with ether to yield unchanged piperidinol (3·9 g., m. p. 159—160°). Treatment of the filtrate with hydrogen chloride yielded 4-hydroxy-4-phenylpiperidine hydrochloride together with a hydrochloride (3 g.), m. p. 182—183°, identical with that described in (*a*).

Attempted propionation of 1-(2-diphenylmethoxy-3-phenoxypropyl)-1 : 2 : 3 : 6-tetrahydro-4-phenylpyridine with propionic anhydride (containing a few drops of concentrated sulphuric acid), at 100° for several hours or under reflux for a short period, yielded unchanged material as the only identifiable product. Similarly, attempted esterification with propionic acid–pyridine–benzenesulphonyl chloride [17] proved unsuccessful.

3-*Phenoxy*-2-*propionoxypropyl chloride* had b. p. 149—152°/3·5 mm. (Found: C, 59·4; H, 6·4; Cl, 14·7. $C_{12}H_{15}O_3Cl$ requires C, 59·4; H, 6·2; Cl, 14·6%).

Reaction of 3-*Phenoxy*-2-*propionoxypropyl Chloride with* 4-*Hydroxy*-4-*phenylpiperidine*.—A mixture of 4-hydroxy-4-phenylpiperidine (17·7 g., 0·1 mole) and 3-phenoxy-2-propionoxypropyl chloride (12·15 g., 0·05 mole) was heated with stirring until homogeneous, then at 100° for 48 hr. The melt was boiled with ethyl acetate to remove insoluble 4-hydroxy-4-phenylpiperidinium chloride (9·3 g.). Concentration of the extract followed by distillation of the residue at 0·5 mm. yielded fractions: (i) unchanged 3-phenoxy-2-propionoxypropyl chloride (5·6 g., b. p. 122—140°); (ii) 3·2 g., b. p. 150—195°; (iii) 5 g., b. p. 224—228°, and (iv) 5 g., b. p. 230—236°. Fraction (ii) on treatment with ether yielded 4-hydroxy-4-phenyl-1-propionylpiperidine (1·5 g., m. p. 173—174°, after crystallisation from aqueous ethanol, not depressed in admixture with authentic material). Fractions (iii) and (iv) on treatment with ether followed by fractionation of the resultant solids from aqueous ethanol yielded 4-hydroxy-1-(2-hydroxy-3-phenoxypropyl)-4-phenylpiperidine (3·4 g.), m. p. 119—120° not depressed on admixture with an authentic specimen), and a further quantity (1·0 g.) of 4-hydroxy-4-phenyl-1-propionylpiperidine.

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[17] Brewster and Ciotti, *ibid.*, 1955, **77**, 6214.

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227. *The Constitution of Xylan from the Green Seaweed* Caulerpa filiformis.

By I. M. Mackie and Elizabeth Percival.

After alcoholic and aqueous extraction of *Caulerpa filiformis*, dilute alkaline extraction of the residual weed affords a xylan. Methylation and other studies provide evidence for a structure comprising chains of β-D-xylopyranose residues linked between $C_{(1)}$ and $C_{(3)}$.

Comparatively little is known about the polysaccharides of the green seaweeds. Water-soluble materials from *Cladophora rupestris* [1] and from *Ulva lactuca* [2] consist of complex polysaccharide material containing a wide variety of sugar residues. In spite of repeated fractionation with various reagents, no separation of these materials was achieved. Chloroform extraction of acetylated cladophoran did, however, give a small yield of a glucose-rich fraction. Preston and his colleagues,[3] examining the cell-wall material of a number of green seaweeds by *X*-ray and hydrolytic methods, have also revealed the complexity of their polysaccharide constituents.

After removal of water-soluble sulphated polysaccharide material (which contains glucose, galactose, mannose, xylose, rhamnose, and uronic acid residues) from the green seaweed, *Caulerpa filiformis*, mild treatment of the insoluble residue with chlorite [4] was followed by extraction with dilute sodium hydroxide solution at room temperature. Acidification of the alkaline extract afforded a crude xylan (*ca.* 5·0% of the dried weight of weed) (Ash, 2·0; SO_4^{2-}, 3·6%) comprising xylose (90%) and glucose (10%). Precipitation with various copper salts [1,5,6] or with Cetavlon [7] failed to reduce the glucose content, but extraction with water and dialysis afforded xylan (B) (4·5%) containing *ca.* 4% of glucose (ash, 0·5%; SO_4^{2-}, nil). A pure xylan (C) (3·3% dried weight of weed) devoid of glucose and sulphate residues was isolated after exhaustive extraction of material (B) with water. In view of the limited quantity of weed available, and the loss of xylan during complete purification, large-scale investigations were carried out on polysaccharide (B). The extraction of the weed and its treatment with chlorite were carried out under mild conditions in order to minimise the possible degradation of the xylan. During the purification no obvious signs of degradation were apparent; in particular the specific viscosities and periodate consumption of xylan (B) and xylan (C) were similar.

Xylan (B) afforded 92% of crystalline D-xylose on hydrolysis. By two series of five methylations, each with methyl sulphate and sodium hydroxide in an atmosphere of nitrogen,[5] a methylated xylan was prepared containing 31·5% of methoxyl. Four treatments with Purdie's reagents gave a product containing 37·2% of methoxyl. Fractionation using chloroform–light petroleum separated a negligible quantity of lower methylated material (OMe, 22%). The major fractions (OMe, 37—37·4%) were recombined and methylated with sodium and methyl iodide in liquid ammonia.[8] The isolated material had $[\alpha]_D^{18}$ −60° and contained 37·8% of methoxyl (Calc. for $C_7H_{14}O_4$: OMe, 38·7%). Repeated methylation and dialysis had not apparently degraded the xylan seriously, since a xylan acetate prepared by mild acetylation had a specific viscosity of the same order as had the methylated xylan measured under identical conditions.

The methylated xylan was hydrolysed with methanolic hydrogen chloride giving the glycosides, and from them the methylated sugars were obtained by hydrolysis with dilute

[1] Fisher and Percival, *J.*, 1957, 2666.
[2] Brading, Georg-Plant, and Hardy, *J.*, 1954, 319.
[3] Cronshaw, Myers, and Preston, *Biochim. Biophys. Acta*, 1958, **27**, 89.
[4] Wise, *Ind. Eng. Chem. Anal.*, 1945, **17**, 63.
[5] Chanda, Hirst, Jones, and Percival, *J.*, 1950, 1289.
[6] Erskine and Jones, *Canad. J. Chem.*, 1956, 821.
[7] Bera, Foster, and Stacey, *J.*, 1955, 3788.
[8] Hodge, Karjala, and Hilbert, *J. Amer. Chem. Soc.*, 1951, **73**, 3312.

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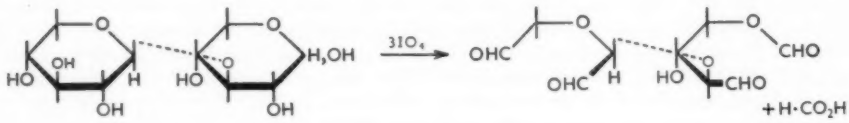
hydrochloric acid. Separation on a cellulose column gave the following molar percentage separation of methylated xyloses: 2 : 3 : 4-tri-*O*-methylxylose (2·9), 2 : 4-di-*O*-methylxylose (95·2) and a mixture of 2- and 4-monomethylxylose (1·9). Both the tri- and the di-*O*-methyl sugars were crystalline. The amount of trimethylxylose corresponds to one non-reducing end group for every 34 xylose residues, but this figure can only be regarded as very approximate as the weight of each fraction was recorded after extensive purification. The value of one non-reducing end group for every 47 anhydro-xylose units (average of two experiments), determined on the methylated hydrolysate by hypoiodite oxidation after separation on a paper chromatogram,[5] is probably a more accurate figure. The presence of monomethylxylose (*ca.* 1·9%) is easily accounted for on the grounds of under-methylation, and of demethylation during hydrolysis. Taken as a whole the methylation results show that the xylan is made up of linear chains of 1 : 3-linked β-D-xylopyranose residues, and that the majority, at least, of the chains are unbranched; the β-configuration being inferred from the negative rotation.

Periodate-oxidation studies were undertaken to obtain further evidence on the constitution of this polymer. A linear 1 : 3-linked xylan, with a reducing group at one end of the molecule, would be attacked by periodate only at the ends of the chains with the reduction of 3 mols. of periodate and the formation of 1 mol. of formic acid and a stable formyl ester, but no formaldehyde.[9] On this assumption the consumption of one mol. of



periodate for about 14 xylose units gives an average chain length of 42, and the yield of formic acid gives a similar figure, since about 1 mol. of formic acid is liberated from 43 xylose units. The small yield of formaldehyde may be due to a small amount of hydrolysis of the formyl ester during the oxidation. On the other hand it is very probable that during the extraction of the xylan with alkali some modification of the reducing group takes place. In the absence of definite knowledge regarding the nature of this group the interpretation of the periodate oxidation results can only be regarded as tentative. The liberation of free xylose (90%) on acid hydrolysis of the oxopolysaccharide does, however, provide further evidence for a 1 : 3-xylosidic linkage.[10]

The contaminating glucose in xylan (B) was separated from the methylated hydrolysate as 2 : 3 : 4 : 6-tetra-*O*-methylglucose (trace, paper chromatography), crystalline 2 : 4 : 6-tri-*O*-methylglucose, and a small quantity of 4 : 6-di-*O*-methylglucose. Taken in conjunction with the small change in rotation of the xylan, on removal of this glucan, all the evidence points to this polymer's being of the laminarin type with 1 : 3-β-linked glucopyranose units. The periodate consumption of such a molecule would be of the same order as that of the xylan, since again only the end residues are liable to attack by this reagent. Evidence for this is the very similar uptake of periodate by xylan (B) (containing 4% of glucose) and by xylan (C) which is glucose-free.

Bearing in mind all the results it seems justifiable to assign to the xylan from *Caulerpa filiformis* a structure containing linear chains of D-xylopyranose units joined by 1 : 3-β-linkages.

Although xylose is a constituent of the polysaccharides of many green seaweeds [3] this is the first time a pure xylan has been isolated from this source. 1 : 4-β-Linked xylans constitute the major polysaccharide of the hemicelluloses of land plants and a xylan containing 80% of 1 : 4-linked and 20% of 1 : 3-linked β-D-xylopyranose units has been

[9] Hough, Taylor, Thomas, and Woods, *J.*, 1958, 1212.
[10] Hough and Perry, *Chem. and Ind.*, 1956, 768.

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separated from the red seaweed, *Rhodymenia palmata*.[11] The present xylan is unique in consisting solely of 1 : 3-linked residues.

Experimental

Paper partition chromatography was carried out on Whatman No. 1 filter paper. Paper ionophoresis was in borate buffer (pH 10) at 750 v for 5 hr. Evaporations were carried out at 40°/15 mm.

The green seaweed, *Caulerpa filiformis*, collected from rock pools near Cape Town in February, 1957, was kindly made available to us by Dr. A. M. Stephen and Mr. R. H. Simons. The weed was dried at 60° and ground to a pale green powder. Extraction of this dried powder (15 g.) with 80% aqueous alcohol under reflux removed most of the colouring matter. Chromatographic examination of the alcoholic extract, after deproteinisation [12] and deionisation,[13] indicated the presence of sucrose and glucose. The residual weed was extracted with dilute hydrochloric acid (pH 3—4) at 70° for 6 hr. (twice) and the combined extracts, after dialysis and freeze-drying, gave an off-white powder (Found: N, 2·5%). Subsequent extracts were therefore treated with trichloroacetic acid before dialysis. After several days the precipitated protein was removed on the centrifuge and the supernatant liquid dialysed against running water for several days. Concentration of the dialysed solution followed by freeze-drying gave an off-white powder (1·5 g.), $[\alpha]_D$ +120° (*c* 3·0 in water) [Ash (direct), 13·5; (as sulphate), 15·4; SO_4^{2-} in ash, 3·8% of dry weight of polysaccharide; total SO_4^{2-}, 7·5; uronic anhydride, *ca.* 8; N, 1·5%].

Chromatography of the hydrolysate (N-sulphuric acid at 100° for 4 hr.) by the method of Flood, Hirst, and Jones [14] (*a*) and of Pridham [15] (*b*) showed that the polysaccharide material contained the following approximate molar proportions of the sugars: galactose (*a*) 4, (*b*) 4; glucose (*a*) 14, (*b*) 15; mannose (*a*) 2, (*b*) 2; xylose (*a*) 2, (*b*) 1; and rhamnose (*a*) 0·5, (*b*) 0·2. The presence of anhydro- and/or ketose sugar residues in the hydrolysate and in the polysaccharide was indicated by the red colour given by a Seliwanoff test,[16] and the yellow-brown spots produced on filter paper with the anthrone reagent.[17] Extraction with cold and hot water and with 0·5% sodium carbonate solution of the alcohol-extracted weed gave similar polysaccharide material (visual chromatographic examination of the hydrolysate).

Extraction of a Xylan.—The residual weed (from 50 g. of original dried weed), after extraction with alcohol and dilute acid, was heated to 70° in water (250 c.c.) containing glacial acetic acid (1 c.c.) and sodium chlorite [4] (4 × 3 g.) was added at hourly intervals during 4 hr. The weed was then separated at the centrifuge, washed with water and extracted with N-sodium hydroxide (125 c.c.) at room temperature with stirring during 3 days. The alkaline solution, freed from weed, was acidified with glacial acetic acid to pH 5. A gel-like precipitate was deposited which was washed with water to remove acid, followed by alcohol of increasing concentration and finally with ether. The white, powdery solid (2·5 g.), after drying over phosphoric oxide in a vacuum-desiccator, had $[\alpha]_D$ −28° (*c* 0·8 in 0·1N-NaOH) (Ash, 2·0; SO_4^{2-}, 3·6%). Hydrolysis and quantitative chromatography [14] showed that the polysaccharide contained xylose (90%) and glucose (10%).

Purification of the Xylan.—The xylan was precipitated from alkaline solution as the copper complex with Fehling's solution,[5] with copper acetate,[6] and with Benedict's solution.[1] Precipitation was also brought about with 10% aqueous cetyltrimethylammonium bromide.[7] Hydrolysates from each of the regenerated xylans contained *ca.* 10% of glucose. Suspension of the crude polysaccharide (5 g.) in water (500 c.c.) with agitation for 24 hr. gave on filtration and drying a white powder (A) (4·75 g.), $[\alpha]_D$ −31° (*c* 0·5 in 0·5N-NaOH) (Found: SO_4^{2-}, 2·4%). After dialysis against running water for 4 days the polysaccharide (4·5 g.) was isolated by freeze-drying of the aqueous suspension. This material (B) was devoid of sulphate and contained xylose 95%,[15] 97%,[14] and glucose 5%,[15] 3% [14] (ash, 0·5%). Crystalline xylose, m. p. and mixed m. p. 143—144°, $[\alpha]_D$ +41·9° (*c* 0·9), was separated from the hydrolysate in 92% yield. This

[11] Chanda and Percival, *Nature*, 1950, **166**, 787.
[12] Laidlaw and Reid, *J. Sci. Food Agric.*, 1952, **3**, 19.
[13] Anderson and Wylam, *Chem. and Ind.*, 1956, 191.
[14] Flood, Hirst, and Jones, *J.*, 1949, 1659.
[15] Pridham, *Analyt. Chem.*, 1956, 1967.
[16] Seliwanoff, *Ber.*, 1887, **20**, 181.
[17] Johanson, *Nature*, 1953, **172**, 956.

was further characterised as the dibenzylidene dimethyl acetal derivative, m. p. mixed m. p. 210°. Repeated extraction of polysaccharide (B) (1·5 g.) with water finally led to the isolation of xylan (C) (1·1 g.), $[\alpha]_D$ −35°, containing only xylose residues.

Periodate Oxidation of Xylan.—(i) *Uptake of periodate.* Dry xylan (B) (361 mg.), (C) (312·4 mg.) was oxidised with 3% sodium metaperiodate (50 ml.) in the dark and the reduction of periodate was measured.[18] The moles of periodate consumed per $C_5H_8O_4$ unit were determined: (B) 0·015 (3 hr.), 0·026 (5 hr.), 0·055 (22 hr.), 0·064 (42 hr.), 0·070 (66 hr.), 0·070 (114 hr. const.). (C) 0·021 (5 hr.), 0·040 (11 hr.), 0·045 (24 hr.), 0·072 (48 hr.), 0·074 (70 hr.), 0·074 (96 hr. const.). The completely oxidised solution (170 hr.), after destruction of excess of periodate with ethylene glycol, was dialysed against distilled water until free from inorganic ions (3 days) and concentrated at 35°/15 mm. to 10—15 c.c. The oxopolysaccharide from (B) (337·8 mg., 98%), isolated from this solution by freeze-drying, was hydrolysed with N-sulphuric acid. The resulting syrup contained xylose [14] (304 mg.) and a trace of glucose.

(ii) *Determination of formic acid released.* Dry xylan (B) (498 mg.) was weighed into a dark stoppered bottle and treated with sodium metaperiodate (50 c.c.; 0·1871M) with continuous agitation. Samples (5 c.c.) were removed at intervals, treated with ethylene glycol (1 c.c.), and titrated with 0·01N-sodium hydroxide from a micro-burette (Methyl Red). The following results (moles × 10^{-2}) of $H{\cdot}CO_2H$ per $C_5H_8O_4$ unit were obtained: 1·5 hr., 0·37; 3 hr., 0·37; 22 hr., 0·75; 46 hr., 1·1; 94 hr., 1·6; 166 hr., 2·1; 262 hr., 2·3; 298 hr., 2·35; 324 hr., 2·4.

(iii) *Formaldehyde release.* Dry xylan (B) (189·6 mg.) was oxidised with sodium metaperiodate (50 c.c.; 0·025M) and the μg. of formaldehyde released measured at intervals: [19] 1 hr., 1·8; 5 hr., 2·6; 23 hr., 5·9; 48 hr., 9·7; 72 hr., 10·6.

Reducing Power of the Xylan.—Hypoiodite oxidation. The polysaccharide (B) (100 mg.) in water was treated with 2N-sodium hydroxide (10 c.c.), followed by 0·1N-iodine (10 c.c.), and the reducing power measured as for the esparto grass xylan.[5] This gave a value of one reducing group per 60 xylose residues.

Methylation of Xylan.—The polysaccharide (B) (8·0 g.) was methylated by sodium hydroxide and methyl sulphate.[5] After two series of five methylations the product was a white powder (8·7 g.; OMe, 31·5%). This partly methylated material was subjected to four further methylations with methyl iodide and silver oxide. The dried (over P_2O_5 to constant weight) white powder (Found: OMe, 37·2; Calc. for $C_7H_{12}O_4$: OMe, 38·75%) had $[\alpha]_D$ −61° (*c* 1·0 in $CHCl_3$).

Fractionation of the Methylated Xylan.—The methylated xylan (4·2 g.) was fractionated by various mixtures of chloroform and purified light petroleum (b. p. 65—66°). The material started dissolving in 20 : 80 chloroform–light petroleum and was completely soluble in a 35 : 65 mixture. The results are given below:

Fraction	Solvent chloroform–light petroleum	Yield (mg.)	OMe	$[\alpha]_D$
1	0 : 100	0	—	—
2	20 : 80	15	22·1	−26°
3	25 : 75	43	37·0	−61
4	30 : 70	727	37·4	−62
5	35 : 65	2560	37·1	−62

Fractions 3—5 were recombined.

Methylation in Liquid Ammonia.—The above combined fractions 3—5 (3·3 g.) were thoroughly dried and introduced into a flask, fitted with a stirrer, which could be sealed against the atmosphere.[9] Ammonia (200 c.c.) was condensed in the flask, and metallic sodium (240 mg.) was added with stirring. After 15 min. methyl iodide (1·0 c.c.) was added. Four further additions of sodium and of methyl iodide were made alternately at 15 min. intervals. The ammonia was allowed to evaporate at room temperature (2 hr.) and then at 50° (1 hr.). Sodium iodide and sodium amide were dissolved by the dropwise addition of water (50 c.c.), and the methylated polysaccharide extracted with chloroform (3 × 100 c.c.). It was precipitated from the dried concentrated chloroform solution as a white powder (2·97 g.) by the addition of ether, and had $[\alpha]_D^{18}$ −60° (*c* 1·0 in $CHCl_3$) and OMe, 37·8%.

Hydrolysis of Methylated Xylan and Separation of Methylated Xyloses.—(a) *By paper chromatography.* The polysaccharide (60 mg.) was treated with 3% methanolic hydrogen chloride (10 c.c.) under reflux for 18 hr., and then hydrolysed with N-hydrochloric acid (10 c.c.) for 18 hr.

[18] Halsall, Hirst, and Jones, *J.*, 1947, 1399, 1427.

at 100°. After neutralisation with silver carbonate the filtrate was de-ionised with Amberlite IR120(H) and IR45(OH) resins. The clear solution was concentrated to a syrup which crystallised completely overnight. Chromatography with butanol–ethanol–water (4 : 1 : 5), and development with aniline oxalate, showed three main spots having R_G 0·94, 0·66, and 0·40, identical with 2 : 3 : 4-tri-*O*-methylxylose, 2 : 4-di-*O*-methylxylose, and a mono-*O*-methylxylose respectively. A fourth faint buff-coloured spot, R_G 0·76, was also detected. This is shown later to be due to a trimethyl-glucose.

The methylated pentoses were estimated by alkaline hypoiodite after separation on the paper chromatogram: [5]

Sugar	Wt. (mg.)	Molar composition (%)
2 : 3 : 4-Tri-*O*-methylxylose	0·43; 0·42	2·2; 2·1
2 : 4-Di-*O*-methylxylose	17·78; 17·66	96·5; 96·6
Mono-*O*-methylxylose	0·23; 0·21	1·3; 1·2

(b) *By the cellulose column.* Methylated xylan (2·87 g.) was boiled gently under reflux with 3% methanolic hydrogen chloride (300 c.c.), and the rotation observed: $[\alpha]_D$ −62° (initial) ⟶ +65° (6 hr., constant). After neutralisation with silver carbonate the filtrate was concentrated to a syrup at 35°/15 mm. This was hydrolysed with N-hydrochloric acid (300 c.c.) at 95° and then had α_D +26° (18 hr. constant). Neutralisation of the cooled solution with silver carbonate, followed by deionisation of the filtrate with hydrogen sulphide and Amberlite resins IR120 and IR45 and concentration, gave crystals (2·085 g.). The crystals, dissolved in water, were mixed with cellulose powder and the whole was freeze-dried. The freeze-dried material was packed on top of a cellulose column (3·6 × 70 cm.) which was eluted with light petroleum (b. p. 100—120°)–butan-1-ol (7 : 3) saturated with water. After 9·5 l. had been collected the solvent was changed to butan-1-ol (100 c.c.) and to butan-1-ol half saturated with water in order to elute the monomethylxylose more quickly. After another 1·5 l. had been eluted the column was washed with water. Six fractions were collected. The fractions were weighed after filtration through " Filter Cel," concentration to dryness, dissolution in methanol, filtration, and concentration. The total recovery was 1·813 g. (87%). R_G values were measured in butanol–ethanol–water (4 : 1 : 5), and the chromatograms sprayed with aniline oxalate.

Fraction 1 (340—410 c.c.). <5 mg., R_G 1·0 gave a yellow-brown spot identical with 2 : 3 : 4 : 6-tetra-*O*-methylglucose run as a control.

Fraction 2 (600—820 c.c.), Crystalline 2 : 3 : 4-tri-*O*-methylxylose (57·4 mg.) gave a mauve spot, R_G 0·94, identical with 2 : 3 : 4-tri-*O*-methylxylose. M. p. and mixed m. p. (after recrystallisation from light petroleum) 85—87°, $[\alpha]_D$ +19·8° (*c* 1·1 in H_2O) (Found: OMe, 48·2. Calc. for $C_8H_{16}O_5$: OMe, 48·4%).

Fraction 3 (2·1—2·29 l.). Crystalline 2 : 4 : 6-tri-*O*-methylglucose (15·6 mg. (gave a red brown spot, R_G 0·76, identical with an authentic specimen. M. p. and mixed m. p. 126°, $[\alpha]_D^{15}$ +108° ⟶ +70° (*c* 1·5 in MeOH).

Fraction 3(*a*) (2·29—2·35 l.) (268 mg.). Chromatography showed this to be a mixture of 2 : 4 : 6-tri-*O*-methylglucose and 2 : 4-di-*O*-methylxylose.

Fraction 4 (2·35—4·35 l.). Crystalline 2 : 4-di-*O*-methylxylose (1·433 g.) gave a pink spot, R_G 0·66, identical with an authentic specimen. M. p. and mixed m. p. 116°, $[\alpha]_D^{15}$ −26° ⟶ +28° (*c* 1·0 in H_2O; 24 hr. constant) (Found: C, 47·44; H, 7·77; OMe, 34·3. Calc. for $C_7H_{14}O_5$: C, 47·20; H, 7·86; OMe, 34·8%). It gave an *X*-ray powder photograph identical with that given by authentic material and different from the photograph of 2 : 3-di-*O*-methylxylose.

Fraction 5 (8·3—9·2 l.). Syrupy 4 : 6-di-*O*-methylglucose (8·0 mg., contaminated with wax) gave a brown spot, R_G 0·46, when sprayed with *p*-anisidine hydrochloride, as did authentic material, whereas 2 : 4-di-*O*-methylglucose gave a yellow spot (paper chromatography). Its identity was confirmed by ionophoresis.[20] The M_G values of the different dimethylglucoses are: 2 : 4-di-*O*-methyl, 0·09; 2 : 6-di-*O*-methyl, 0·05; 3 : 4-di-*O*-methyl, 0·35; 4 : 6-di-*O*-methyl, 0·2; 3 : 6-di-*O*-methyl, 0·65; 2 : 3-di-*O*-methyl, 0·10.

Fraction 6 (10·72—11·0 l.). Syrupy monomethylxylose (31·5 mg.) had $[\alpha]_D^{15}$ +19° (*c* 3·1 in H_2O) and gave a pink spot, R_G 0·40, with aniline oxalate (Found: OMe, 17·4. Calc. for $C_6H_{12}O_5$: OMe, 18·9%). Paper chromatography in butan-1-ol–pyridine–water (10 : 3 : 3) gave two spots, $R_{Rhamnose}$ 1·19 and 1·10, corresponding to authentic 2- and 4-*O*-methylxylose respectively. Spraying with *p*-anisidine hydrochloride gave a mauve spot with the 2-*O*-methyl

[19] Hough, Powell, and Woods, *J.*, 1956, 4799.
[20] Foster, *Chem. and Ind.*, 1952, 1050.

sugar and a reddish-brown spot for the 4-*O*-methyl sugar. Ionophoresis gave two distinct spots, M_G 0·40 for 2-*O*-methylxylose and 0·25 for the 4-*O*-methylxylose.

The water-washings were devoid of carbohydrate material.

Acetylation of Xylan (*B*).—Xylan (2·4 g.) was acetylated as for esparto grass xylan [5] except that the pyridine solution was cooled to 0° before addition of acetic anhydride and the product, after thorough washing with water, was isolated by freeze-drying of its suspension in water. A second acetylation gave a white powder (2·75 g.) which was insoluble in methanol, ethanol, acetone, or chloroform, and had $[\alpha]_D$ −51° (*c* 0·4 in *m*-cresol) (Found: Ac, 39·5. Calc. for $C_9H_{12}O_6$: Ac, 39·8%).

Viscosity Determinations of Xylan and its Derivatives.—The viscosities of xylan in 0·5N-sodium hydroxide and its derivatives in *m*-cresol were measured in Ostwald viscometers Nos. 1 and 2 respectively at 20°. The results are tabulated.

		Average time of flow (sec.)		
	c	Solution	Solvent	η_{sp}/c *
Xylan (B)	0·0435	287·8	237·3	4·89
Xylan (C)	0·0381	283·3	237·3	5·01
Acetylated xylan	0·0191	319·4	238·0	17·96
Methylated xylan	0·0316	345·4	238·0	14·29

* *c* represents concentration of $C_8H_8O_4$ units.

The authors are grateful to Professor E. L. Hirst, F.R.S., C.B.E., for his interest and advice, the Institute of Seaweed Research for a maintenance grant (to I. M. M.), and the Distillers Company Limited and Imperial Chemical Industries Limited for grants.

Department of Chemistry, University of Edinburgh. [*Received, November 17th*, 1958.]

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228. *Kinetics of the Bromination of* m-*Nitrophenol in Aqueous Solution.*

By R. P. Bell and T. Spencer.

Kinetic measurements have been made of the bromination of *m*-nitrophenol in aqueous solution. The initial concentrations of phenol and bromine were respectively about 3×10^{-4}M and 10^{-5}M, and the disappearance of bromine was followed by measuring the limiting current at a rotating platinum cathode. Velocity constants are derived for the reactions of bromine with the *m*-nitrophenol molecule and anion, and for the reaction of the tribromide ion with the *m*-nitrophenol anion.

Little kinetic information is available about the rapid reaction between phenols and bromine in aqueous solution. Francis [1] studied the relative rates of bromination of different phenols by competition methods, but his results cannot be interpreted in any simple manner since he used solutions of varying acidity and did not take into account the widely different reactivities of the phenol molecule and the phenoxide ion. Robertson, de la Mare, and Swedlund [2] report direct measurements of the rate of bromination of phenol in acetic acid solution, and estimate that the hydroxyl group activates the benzene ring by a factor of 10^{11}. In these measurements the main reactive species is certainly the undissociated phenol molecule, since the solvent is strongly acidic and the addition of sulphuric acid does not decrease the rate. Recent work on the iodination of phenol [3] involves iodination by an iodine cation, the iodine molecule being inactive.

This paper deals with bromination in aqueous solution under conditions where Br_2 and Br_3^- are the only effective agents, and measurements over a range of acidity make it possible to separate the contribution of the phenol molecules and the phenoxide ions.

[1] Francis, *J. Amer. Chem. Soc.*, 1925, **47**, 2211, 2340.
[2] Robertson, de la Mare, and Swedlund, *J.*, 1953, 782.
[3] Berliner, *J. Amer. Chem. Soc.*, 1951, **73**, 4307.

The use of an electrical method for following the bromine concentration makes it possible to work with concentrations 10^{-4}—10^{-6}M and to follow reactions with half-times of a few seconds. Even so, the reaction of phenol itself with bromine was too fast to measure, and it was necessary to use the less reactive *m*-nitrophenol.

Experimental

m-Nitrophenol, recrystallised from carbon disulphide, had m. p. 96·5—97°. 2-Bromo-3-nitrophenol, prepared by direct bromination as described by Linden [4] and recrystallised twice from water, had m. p. 147°. Inorganic reagents were " AnalaR " or of pure quality. The acidity was fixed by adding perchloric acid, and bromide was added as sodium bromide on account of the low solubility of potassium perchlorate.

The decrease in bromine concentration was followed polarographically by measuring the limiting current between a rotating platinum cathode and a stationary platinum anode, as described by Kolthoff and his co-workers.[5,6] The cathode was of platinum wire 0·5 mm. in diameter and 7 mm. long and projected horizontally near the bottom of a vertical glass shaft which rotated at a constant speed of 560 revolutions per min. The shaft terminated in a single-bladed glass stirrer which mixed the reactants. The anode was of platinum gauze, 2 × 2 cm., and was fixed horizontally a short distance below the stirrer. The reaction vessel was a 150 c.c. beaker and 100 c.c. of reaction mixture were used. A potential of 0·2 v (corresponding to the flat part of the polarographic curve) was applied across the electrodes, and the current measured directly by a mirror galvanometer, resistance 40 ohms, period 2 sec., full sensitivity 200 mm./μA. For some of the fastest reactions a Cambridge " Flik " galvanometer was used, having a period of 0·2 sec. and a full sensitivity of 100 mm./μA. In each experiment the sensitivity was adjusted by a shunt so that the initial bromine concentration gave a full-scale deflection. All measurements were made at 25° ± 0·01°. Tests showed that under these conditions the galvanometer deflection is a linear function of the bromine concentration in the range 10^{-4}—10^{-6}M: the absolute bromine concentrations are not required here since the reactions are of first order. This method of following the bromine concentrations is more accurate than the method previously described [7] based on redox potentials, though it will not cover such a wide concentration range. After being used for some time the electrodes often become unresponsive to changes in bromine concentration (cf. Lingane and Anson [8]). This could usually be cured by cleaning with hot concentrated nitric acid, but in extreme cases it was necessary to heat the electrodes to bright redness and to re-make them.

The reaction mixtures contained initially about 3×10^{-4}M-phenol and 10^{-5}M-bromine The reaction was started by adding a small quantity of phenol solution from a syringe to a solution containing bromine, sodium bromide, and perchloric acid. Galvanometer readings were taken at intervals of 2—10 sec., a calibrated metronome being used for the faster reactions. The course of the reactions was of strictly first order up to at least 90% of reaction, and the apparent first-order velocity constants were obtained by plotting log $(r_\infty - r_t)$ against t, where r is the galvanometer reading at time t. Second-order constants were then obtained by dividing the first-order constants by the phenol concentration. These second-order constants had to be corrected for the subsequent bromination of the 2-bromo-3-nitrophenol first formed, since although this compound reacts more slowly than *m*-nitrophenol it is a stronger acid and is therefore present to a greater extent as the reactive anion. The rate of bromination of 2-bromo-3-nitrophenol was measured under the same conditions of acidity and bromide concentration, and the observed velocity with *m*-nitrophenol was corrected by subtracting the velocity corresponding to the amount of 2-bromo-3-nitrophenol present at 50% of reaction. Kinetic analysis shows that this procedure is legitimate when the correction is small, and in our experiments it ranged between 5% and 15%. It was not possible to obtain reliable velocity constants for low values of $[H^+]$ or $[Br^-]$, since under these conditions the correction becomes too large. The corrected constants are given in the Table.

[4] Linden, *Ber.*, 1885, **18**, 612.
[5] Laitenen and Kolthoff, *J. Phys. Chem.*, 1941, **45**, 1079.
[6] Kolthoff and Reynolds, *Discuss. Faraday Soc.*, 1954, **17**, 167.
[7] Bell and Ramsden, *J.*, 1958, 161.
[8] Lingane and Anson, *Analyt. Chem.*, 1956, **28**, 1871.

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Bromination of m-*nitrophenol at* 25°.

Velocity constants in l. mole^{-1} sec.$^{-1}$, corrected for second-stage bromination. Calculated values in parentheses.

[$HClO_4$]		0·06	0·2	0·5	1·0
[NaBr]	0·025	178 (179)	101 (104)	80 (80)	64 (70)
	0·05	138 (140)	76 (81)	61 (61)	53 (54)
	0·1	107 (101)	56 (57)	44 (42)	41 (37)
	0·15	78 (80)	44 (44)	34 (33)	29 (28)
	0·2	67 (68)	36 (37)	25 (27)	25 (23)

Discussion

Under our conditions the most likely brominating agents are Br_2 and Br_3^-. Hypobromous acid will be present only in very small amounts, because of the high concentration of hydrogen ions and bromide ions: it is in any case a much less effective reagent than molecular bromine.[1,9] Similarly, the conditions are unfavourable for the presence of kinetically significant quantities of a cationic bromine species. The fact that the rate is decreased by an increase in the concentration of either bromide ions or hydrogen ions shows that Br_2 is more reactive than Br_3^-, and that the nitrophenoxide anion is more reactive than the undissociated molecule. Actually the experimental results provide no evidence for any reaction between the two least reactive species, Br_3^- and phenol molecule, and can be accounted for quantitatively in terms of the three reactions phenol + Br_2, phenoxide ion + Br_2, and phenoxide ion + Br_3^-. If the second-order velocity constants for these reactions are k_1, k_2, and k_3 respectively, the observed velocity constant k is given by

$$k(1 + K[Br^-]) = k_1 + K_a(k_2 + k_3K[Br^-])/f_\pm^2[H^+] \quad . \quad . \quad . \quad . \quad (1)$$

where K_a is the dissociation constant of *m*-nitrophenol ($5{\cdot}3 \times 10^{-9}$),[10] and K the equilibrium constant $[Br_3^-]/[Br_2][Br^-] = 18$.[11] The activity coefficient $f_\pm$ refers to the ions of *m*-nitrophenol, but in the absence of information about these we have used the values for perchloric acid. The values in parentheses in the Table are calculated from

$$k(1 + 18[Br^-]) = 91 + (6{\cdot}9 + 12[Br^-])/f_\pm^2[H^+] \quad . \quad . \quad . \quad . \quad (2)$$

and comparison with eqn. (1) gives the following velocity constants, all in l. mole^{-1} sec.$^{-1}$: *m*-$NO_2{\cdot}C_6H_4{\cdot}OH + Br_2$, $k_1 = 91$; *m*-$NO_2{\cdot}C_6H_4{\cdot}O^- + Br_2$, $k_2 = 1{\cdot}3 \times 10^9$; *m*-$NO_2{\cdot}C_6H_4{\cdot}O^- + Br_3^-$, $k_3 = 1{\cdot}3 \times 10^8$. The value of k_1 is higher than that found by Robertson, de la Mare, and Swedlund [2] for phenol itself in acetic acid, but the change of solvent would account for a discrepancy in this direction. k_2 represents an extremely fast reaction, and is of the same order of magnitude as previously found for the reaction of bromine and iodine with enolate ions [12,13,14] and of bromine with *NN*-dialkylanilines.[7] It seems likely that a second-order velocity constant of 10^9—10^{10} l. mole^{-1} sec.$^{-1}$ represents an upper limit for reactions in aqueous solution, and that none of these reactions involves any appreciable energy of activation. This would explain why in the present instance the nitro-group exerts no detectable de-activating effect on k_2, though it undoubtedly does so in aromatic species of lower intrinsic reactivity, such as the phenol molecule.

Several investigators have found [15,16] that the tribromide ion has negligible reactivity as a brominating agent compared with the bromine molecule, and we have not been able to detect any reaction between tribromide ion and the molecule of *m*-nitrophenol. On the

[9] Derbyshire and Waters, *J.*, 1950, 564.
[10] Lunden, *Z. physikal. Chem.*, 1910, **70**, 249.
[11] Griffith, McKeown, and Winn, *Trans. Faraday Soc.*, 1932, **28**, 101.
[12] Bell and Spiro, *J.*, 1953, 429.
[13] Bell and Engel, *J.*, 1957, 247.
[14] Bell and Vogelsong, *J.*, 1958, 243.
[15] Bradfield, Davies, and Long, *J.*, 1949, 1389.
[16] Wilson and Soper, *J.*, 1949, 3376.

other hand, there is clear evidence of reaction between tribromide ion and the *m*-nitrophenoxide ion, though the exact value of k_3 is sensitive to the value assumed for the tribromide equilibrium constant. Evidence for the reactivity of tribromide ion has been found in the bromination of the enol and enolate of malonic ester [12] and of *NN*-dialkylanilines,[7] and the tri-iodide ion similarly shows a measurable activity in the iodination of various enols and enolate ions.[13,14] All these reactions have velocity constants in the range 10^4—10^{10}, and it is reasonable that species of such high reactivity should show little discrimination between different halogenating agents: thus iodine and bromine react at closely similar rates with the enol and with the enolate ion of malonic ester, though their reactivities differ greatly towards less reactive organic species. Another example of the same principle occurs in relations between catalytic power and basic strength, where the exponent β in $k_B = GK_B^{\beta}$ decreases steadily with the increasing reactivity of the substrate in a series of ketones and similar substances covering a range of 10^{10} in reaction velocity.[17]

We thank the Department of Scientific and Industrial Research for a grant (to T. S.).

PHYSICAL CHEMISTRY LABORATORY, OXFORD. [*Received, December 11th*, 1958.]

[17] Bell and Lidwell, *Proc. Roy. Soc.*, 1940, *A*, **176**, 88; Bell, Gelles, and Möller, *ibid.*, 1949, *A*, **198**, 308.

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229. *Steroids of Unnatural Configuration. Part I. The Stereochemistry of Lumisterol and 9α-Lumisterol (Pyrocalciferol).**

By J. CASTELLS, E. R. H. JONES, G. D. MEAKINS, and R. W. J. WILLIAMS.

Lumisterol and pyrocalciferol are two of the four ergosterol stereoisomers involving variations in the configurations at the 9- and the 10-position. The preparation from these two sterols of pairs of $C_{(9)}$-epimers and comparison of their molecular rotations indicated that the accepted structures should be reversed, *i.e.*, that lumisterol has the 9β- and pyrocalciferol the 9α-configuration.

This proposal has been confirmed by a procedure involving the elimination of the stereochemical differences at position 10. Degradation of lumisterol yields a tricyclic ketone (XIII, ii) identical with that derived from *iso*pyrocalciferol (9β-ergosterol).

The use of the more systematic names 9β-ergosterol and 9α-lumisterol in place of *iso*pyro- and pyro-calciferol respectively is now desirable.

WHILE studying routes to cortisone from ergosterol we encountered compounds with the unnatural 9β-configuration and made some studies of their properties.[1] One of the most unexpected observations was that a 7 : 8-double bond in such compounds could be hydrogenated without difficulty, whereas in the natural (9α) steroids this linkage is very inert and cannot be reduced directly. This observation emphasised that much of the behaviour regarded as characteristic of steroids is dependent upon the common stereochemistry of the group. It led on to the suggestion that investigations on unnatural steroids might reveal significant chemical and biological variations. Although many such steroids have been prepared, either from naturally occurring compounds or in synthetic work, there has been as yet little systematic study of their properties. Inversion of configuration at position 8, 9, or 10 produces a profound effect on molecular shape, and series of suitable compounds are available from the multifarious transformation reactions of the readily accessible ergosterol. Working with ergosterol stereoisomers has the

* A preliminary account of this work appeared in *Proc. Chem. Soc.*, 1958, 7.

[1] Bladon, Henbest, Jones, Lovell, Wood, and Woods; Elks, Evans, Hathway, Oughton, and Thomas, *J.*, 1953, 2921.

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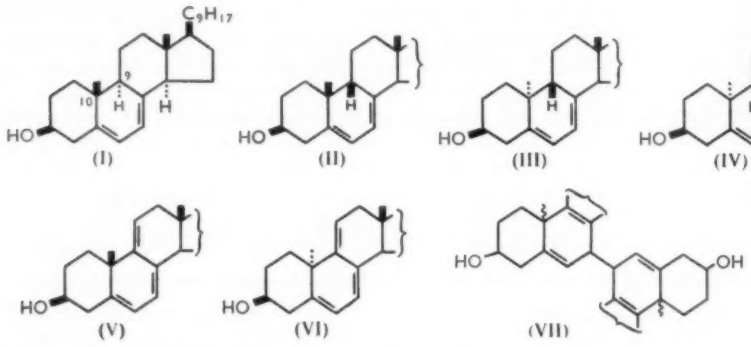
additional advantage that the results obtained can be considered in the light of the extensively known chemistry of the parent " normal " sterol.



Studies have been made [2] of the many partial and complete reduction products of the 9- and the 10-isomers (II—IV) of ergosterol (I), during which doubts accumulated concerning the accepted configurations of lumisterol and pyrocalciferol at position 9. It is therefore necessary at the outset to consider the structures of the parent substances, lumisterol, one of the irradiation products of ergosterol, and pyro- and *iso*pyro-calciferol, formed by thermal cyclisation of calciferol (vitamin D_2).

It is rigorously established [3] that all three are stereoisomers of ergosterol (I), differing only in the configurations at one or both of the centres 9 and 10. The orientations at $C_{(10)}$ are revealed by dehydrogenation of ergosterol and *iso*pyrocalciferol by mercuric acetate to dehydroergosterol (V), and of lumisterol and pyrocalciferol to dehydrolumisterol [4] (VI). Since ergosterol is certainly the 10β-Me : 9α-H-isomer, *iso*pyrocalciferol is unequivocally represented as the 9β-epimer (II).

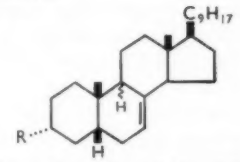
Lumisterol and pyrocalciferol are thus shown to have 10α-methyl groups but formulation of the former as the 9α-compound (IV) and pyrocalciferol as the 9β-isomer (III) was based in a tenuous way on the behaviour of ergosterol and its companions towards irradiation (in the presence of eosin) in the absence of oxygen.[5] Only two (ergosterol and pyrocalciferol) of the four isomers underwent dehydrogenation to give " pinacols " (VII), and on the assumption that an *anti*-arrangement of the 10-methyl group and the 9-hydrogen atom was the necessary condition for pinacol formation, the currently accepted structures were proposed. Although a mechanism for this and similar reactions has been suggested recently [6] the structural features governing pinacol formation are not yet apparent. An *X*-ray analysis [7] of lumisteryl 4-iodo-3-nitrobenzoate was interpreted (electron-density projections only were calculated) as supporting the 9α-representation but the results are not incompatible with a 9β-configuration.[8]

As our studies advanced it became possible to compare the molecular rotations of pairs of compounds, derived from lumisterol and pyrocalciferol, differing only in their configurations at position 9. The preparation of these substances (see Table) will be described in later papers: it is stressed here that all structural details (except the $C_{(9)}$-orientations) were unambiguously determined by methods independent of the stereochemistry at position 9.

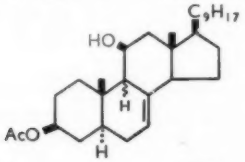
[2] Ph.D. theses of Castells, Fletcher, and Ridley, Manchester, 1955—56.
[3] See summary of evidence in Fieser and Fieser, " Natural Products related to Phenanthrene," 3rd edn., Reinhold Publ. Co., New York, 1949.
[4] Windaus and Dimroth, *Ber.*, 1937, **70**, 376.
[5] Kennedy and Spring, *J.*, 1939, 250.
[6] Owades, *Experientia*, 1950, **6**, 258.
[7] Hodgkin and Sayre, *J.*, 1952, 4561.
[8] Personal communication from Dr. D. M. Hodgkin.

Type (A) Type (B)

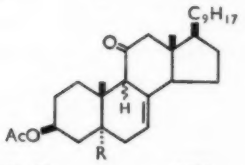
10β-Methyl steroids



Ref.	$[M]_D$	R	Ref.	$[M]_D$	ΔM_D (A − B)
9α-Compounds			9β-Compounds		
a	+171°	OH	*b*	+24°	+147°
a	+260	OAc	*b*	+31	+229

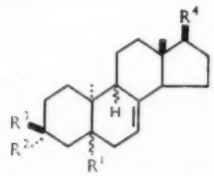


c	−96°		*d*	−395°	+299°



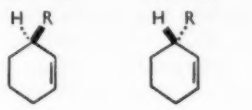
e	+113°	H	*e*	−867°	+980°
e	+430	OAc	*e*	−251	+681

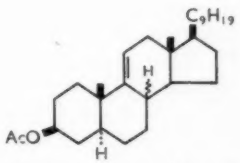
10α-Methyl steroids



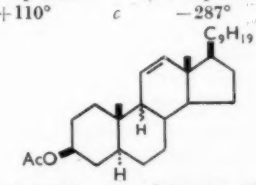
Pyrocalciferol derivs. (9α)			Lumisterol derivs. (9β)	
$[M]_D$	R^2	R^3	$[M]_D$	ΔM_D (A − B)
$R^1 = 5\beta$-H; $R^4 = C_9H_{17}$				
+605°	H	OH	+131°	+474°
+585	H	OAc	+97	+488
+426	H	DNB	+18	+408
+648	OH	H	+179	+469
+689	3-Oxo		+137	+552
$R^1 = 5\beta$-H; $R^4 = C_9H_{19}$				
+617	3-Oxo		+147	+470
$R^1 = 5\alpha$-H; $R^4 = C_9H_{19}$				
+296	H	OH	−24	+320
+203	H	OAc	−141	+344
+125	H	DNB	−220	+345

Type (A) Type (B)



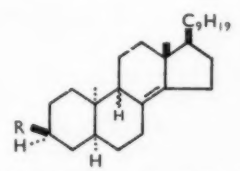


Ref.	$[M]_D$	Ref.	$[M]_D$	ΔM_D (A − B)
9α-Compound		9β-Compound		
c	+110°	*c*	−287°	+397°



8α-Compound		8β-Compound	
f	+477°	*g*	+75° +402°

[a] Barton and Miller, *J.*, 1949, 337. [b] First prepared by Busse, *Z. physiol. Chem.*, 1933, **214**, 211, but $[M]_D$ values taken from unpublished work by Jones, Henbest, and Ridley. [c] Crawshaw, Henbest, Jones, and Wagland, *J.*, 1955, 3420. [d] Deduced from 11α-OH-compound [c] by applying standard correction (Barton and Klyne, *Chem. and Ind.*, 1948, 755). [e] Bladon, Henbest, Jones, Lovell, Wood, Woods, Elks, Evans, Hathway, Oughton, and Thomas, *J.*, 1953, 2921. [f] Bream, Eaton, and Henbest, *J.*, 1957, 1974. [g] Crawshaw, Henbest, and Jones, *J.*, 1954, 731.



Lumisterol derivs. (9β)		Pyrocalciferol derivs. (9α)	
$[M]_D$	R	$[M]_D$	ΔM_D (A − B)
+80°	OH	−252°	+332°
−22	OAc	−305	+283
−59	DNB	−238	+179

DNB = **3** : 5-$(NO_2)_2C_6H_3$·CO·O.

Comparisons were based on Mills's generalisation [9] that, in terpenes with asymmetry at allylic positions, compounds of type (A) have more positive rotations than their enantiomers (B). This relation has been used for structural diagnosis at position 9 in tetracyclic triterpenoids having 7 : 8-double bonds (see the comparison [10] between derivatives of butyrospermol [11] and euphol, and the allocation of configuration to position 9 in masticadienonic acid [12]), and its validity with 10β-methyl steroids is demonstrated by the data in the upper part of the annexed Table of molecular rotations for compounds of established constitution. [The allylic centre is at $C_{(9)}$ in six of the pairs and at $C_{(8)}$ in the remaining pair. Throughout the Table the compounds are arranged to show their relations to structures (A) and (B).]

The ΔM_D values of the 10β-methyl steroids are of the expected (positive) sign, and average about 450 units. (The exceptionally high values of the fourth and fifth pairs probably arise from the presence of oxo-groups adjacent to the allylic centres.) To produce a corresponding result (positive differences, average 390 units) with the lumisterol and pyrocalciferol derivatives it is necessary to adopt a 9β-structure (III) for lumisterol and the 9α-formulation (IV) for pyrocalciferol, *i.e.*, to reverse the previously accepted values. [The appearance of lumisterol (and pyrocalciferol) derivatives on both sides of the Table arises from the differing positions of the olefinic bonds which alter the relations to structures (A) and (B).]

In spite of the strong indication from the molecular-rotation data it seemed desirable to produce independent evidence. This has now been obtained in the manner indicated in the formula scheme (VIII—XIII), all four isomers having been degraded by the same procedure to stereoisomeric tricyclic ketones (XIII), those derived from lumisterol (VIIIc) and *iso*pyrocalciferol (VIIIb) proving identical. Since no opportunities for inversion at the 9-position exist in the series of transformations effected (see below), it follows that lumisterol, having now the same 9-configuration as *iso*pyrocalciferol, must be represented by (III).

Nomenclature (in concurrence with the Editors).—Now that structural certainty has been achieved in this group the names 9β-ergosterol and 9α-lumisterol are to be preferred to *iso*pyro- and pyro-calciferol respectively. The four stereoisomers with their names are therefore:

(I)	(II)	(III)	(IV)
Ergosterol	9β-Ergosterol (formerly *iso*pyrocalciferol)	Lumisterol	9α-Lumisterol (formerly pyrocalciferol)

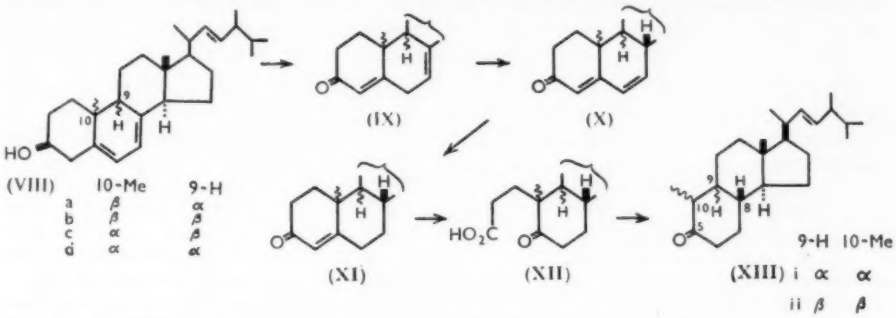
The series of reactions involved in the degradations to the tricyclic ketones were essentially similar with all four sterols and only notable differences will be discussed. The first three stages of Oppenauer oxidation, isomerisation to the 4 : 6-dienone (X), and selective hydrogenation of the 6 : 7-ethylenic bond were carried out mainly according to the highly developed procedure of Ott and his co-workers.[13]

Oppenauer oxidation of 9β-ergosterol (*iso*pyrocalciferol) (VIIIb) gave both the αβ-unsaturated ketone (IXb), and the unisomerised 5 : 7 : 22-trien-3-one (XIV), the mixture being resolved chromatographically. Isomerisation of the homocyclic diene-ketone (XIV) into the αβ-unsaturated isomer (IXb) seemed to proceed only slowly under the normal oxidation conditions.

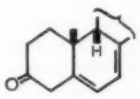
The ketone (IXd) derived from 9α-lumisterol (pyrocalciferol) (VIIId) did not crystallise although it showed ultraviolet absorption of the expected intensity. Fortunately a

[9] Mills, *J.*, 1952, 4976.
[10] Dawson, Halsall, Jones, Meakins, and Phillips, *J.*, 1956, 3172.
[11] Lawrie, Hamilton, Spring, and Watson, *J.*, 1956, 3272.
[12] Barton and Seoane, *J.*, 1956, 4150; Barton, Head, and May, *J.*, 1957, 935.
[13] Shepherd, Donia, Campbell, Johnson, Holysz, Slomp, Stafford, Pederson, and Ott, *J. Amer. Chem. Soc.*, 1955, **77**, 1212.

crystalline conjugated dienone (Xd) was obtained after isomerisation with hydrogen bromide in chloroform–acetic acid. The conjugated dienones (Xb and Xc) derived from 9β-ergosterol and lumisterol were formed along with isomeric ketones (infrared band at



1712 cm.$^{-1}$ indicating unconjugated carbonyl) showing maxima in the region of 2520 Å (ε ~20,000) and obviously containing conjugated diene systems in the B–C–D-ring region [*e.g.*, 8(9) : 14].


(XIV)

It is of course vital that in the processes involved in going from (VIII) to the tricyclic ketones (XIII) no alteration in the stereochemistry at position 9 should occur. This might be the case if the unconjugated dienones (*e.g.*, XIV) or related species were in equilibrium, during the acid-induced isomerisations, with the mono- and fully conjugated di-enones. Such behaviour would be unlikely with normal steroids but could not be ruled out with these " unnatural " isomers. Proof that such equilibria do not exist is available, however, since 9β-lumista- and 9α-lumista-4 : 7 : 22-trienone (IXc and IXd) yield different 4 : 6 : 22-trienones (Xc and Xd); identical products would have resulted if intermediates containing an 8 : 9-double bond had been involved.

Ozonolysis [14] of the unsaturated ketones (XI), the side-chain double bond being protected by bromination, gave the keto-acids (XII). Originally the conversion of the latter into the tricyclic ketones (XIII) was effected in rather poor yields by heating the barium salts,[15] but later pyrolysis of solutions of the sodium salts in molten sodium phenylacetate was employed most advantageously. (We are much indebted to Professor R. B. Woodward for informing us of this improved procedure, worked out in collaboration with Dr. Weesner.) In the case of the keto-acid derived from ergosterol, only one ketone seemed to be formed; no isomerisation could be brought about by acid- or alkali-treatment [16] and it could reasonably be concluded that the 10-methyl group in (XIII, i) must be in the more stable 10α-configuration (*i.e.*, equatorial). Moreover, the pyrolysis of the sodium salt can be regarded as a reversed Michael reaction; [17] the 5 : 10-enolate anion of (XIII) first produced would ketonise to give the 10α-methyl isomer.

From the acids (XIIb and c) derived from 9β-ergosterol (*iso*pyrocalciferol) (VIIIb) and lumisterol (VIIIc) respectively, good yields of the same low-melting tricyclic ketone (XIII, ii) were obtained. Identity was proved by mixed m. p. determinations with both ketones and oximes, by infrared spectra, and by determination of the optical rotatory dispersion curves.* These were identical in form and in the direction of the Cotton effect to that of

* These determinations and many others during this work were made at Wayne University through the good offices of Professor Carl Djerassi. We are much indebted to him for his willing collaboration.

[14] Cf. Turner, *J. Amer. Chem. Soc.*, 1950, **72**, 579.

[15] Turner, *ibid.*, 1954, **76**, 1390.

[16] Cf. the behaviour of 4-methyl-3-oxo-steroids (Sondheimer and Mazur, *J. Amer. Chem. Soc.*, 1958, **80**, 5220).

[17] Cf. Julia, Eschenmoser, Heusser, and Tarköy, *Helv. Chim. Acta*, 1953, **36**, 1885 and references given there.

XUM

the mirror image of the coprostanone curve,[18] thus providing additional confirmation of the *cis*-fusion of rings B/C and the β-configurations at positions 8 and 9 in (XIII, ii).

Further evidence supporting the assignment of the equatorial conformation to the 10-methyl group in the ketones (XIII, i and ii) can be derived from the solvent effects on their rotations. Sondheimer and Mazur[16] have drawn attention to the fact that the rotations of epimerisable (and hence normally axial) α-methyl ketones are considerably lower in methanol or dioxan than in chloroform, whereas little or no solvent effect is observed with the equatorial compounds. The differences with the ketones (XIII) are indicated in the accompanying Table from which it is clear that they support the equatorial assignment.

	1, $[\alpha]_D$ in MeOH	2, $[\alpha]_D$ in $CHCl_3$	Δ(1 − 2)
(XIII, i)	−25° *	−30°	+5°
(XIII, ii)	−44	−48	+4
2α-Methylcholestan-3-one	+31	+32	−1
4α-Methylcholestan-3-one	+25	+26	−1
2β-Methylcholestan-3-one	+67	+86	−19
4β-Methylcholestan-3-one	+16	+36	−20

* In dioxan because of low solubility in MeOH.

The configuration at position 8 in the final products is determined during the isomerisation of the dienone (IX) to the fully conjugated compound (X), and variations would have vitiated the final comparisons between the tricyclic ketones (XIII). Inspection of models indicated that if protonation at $C_{(8)}$ led to the more stable configuration, this would certainly be 8β in three cases; with the ketone derived from 9α-lumisterol (pyrocalciferol) however, no clear indication could be obtained in this way. It is established that 8β-addition occurs in the ergosterol series since progesterone has been obtained[13] from the ketone (XIa) produced by isomerisation. The tricyclic ketone (m. p. 85·5—87°, $[\alpha]_D$ +51·5°) obtained from 9α-lumisterol (pyrocalciferol) was different from that (XIII, i) (m. p. 101—103°, $[\alpha]_D$ −30°) derived from ergosterol. Also the optical rotatory dispersion curve of the former ketone was rather anomalous. We are inclined to suspect stereochemical variation rather at $C_{(8)}$ than at $C_{(10)}$ but, in view of the identity of the ketones from (VIIIb) and (VIIIc) and the attainment of the objective of the investigation, the nature of the difference between the other pair of final products was not further pursued.

With the structures of the parent compounds established it is now possible to interpret the results of a detailed study of the partial and complete reduction products from lumisterol, pyrocalciferol, and *iso*pyrocalciferol. The work will be described in subsequent communications.

Experimental

Rotations were measured for chloroform solutions at room temperature. M. p.s were determined on a Kofler block and are corrected. Ultraviolet light absorption data were obtained with alcoholic solutions. Alumina used for chromatography was Spence's Grade " H; " deactivated alumina refers to Grade " H " to which 5% of 10% acetic acid had been added according to the method of Farrar, Hamlet, Henbest, and Jones.[19] Light petroleum refers to the fraction of b. p. 60—80°.

22 : 23-*Dibromoergost*-4-*en*-3-*one*.—A solution of ergosta-4 : 22-dien-3-one[13] (1·29 g.) in chloroform (250 c.c.) was cooled to −80° and bromine in chloroform (9 c.c.; 2% v/v) was added dropwise with stirring. Triethylamine was added, solvent removed under reduced pressure, and the residue dissolved in ether and filtered; removal of the ether and crystallisation of the residue from ethanol afforded **22 : 23-*dibromoergost*-4-*en*-3-*one*** (1·36 g.), m. p. 195—198°, $[\alpha]_D$ +38° (*c* 0·9) (Found: C, 60·35; H, 8·0; Br, 28·7. $C_{28}H_{44}OBr_2$ requires C, 60·45; H, 7·95; Br, 28·7%), $\lambda_{max.}$ 2390 Å (ε 15,600), $\nu_{max.}$ (Nujol mull) 1681 (conjugated carbonyl) and 1620 (conjugated double bond), no peak at *ca.* 970 (*trans*-CH=CH−) cm.$^{-1}$. Debromination with activated zinc dust gave a high yield of the parent ergosta-4 : 22-dien-3-one, m. p. and mixed m. p. 127—131°, $[\alpha]_D$ +39° (*c* 1·1), $\lambda_{max.}$ 2410 Å (ε 16,800).

[18] Djerassi and Closson, *J. Amer. Chem. Soc.*, 1956, **78**, 3761.
[19] Farrar, Hamlet, Henbest, and Jones, *J.*, 1952, 2657.

XUM

5-*Oxo*-3 : 5-seco-A-*norergost*-22-*en*-3-*oic Acid* (XIIa).—A stream of ozonised oxygen (10 l./hr.; 2%) was passed into 22 : 23-dibromoergost-4-en-3-one (1·45 g.) in " AnalaR " ethyl acetate (15 c.c.) at −80° until a permanent blue colour was produced (50 min.). Nitrogen was then passed in, the solution being allowed to warm to room temperature. " AnalaR " acetic acid (150 c.c.), water (50 c.c.) and 26% hydrogen peroxide (6 c.c.) were added and, after 40 hr., isolation *via* ether furnished an oil which was treated with activated zinc dust (2 g.) in refluxing 1 : 1 ether–methanol (100 c.c.) for 2 hr. More zinc dust (1 g.) was added and refluxing was continued for 1 hr. The hot solution was filtered, the solid being washed with hot methanol and ether; removal of solvents gave an oil to which were added dilute hydrochloric acid and ether. The ethereal layer yielded an oil which was chromatographed on silica gel (80 g.). Benzene and benzene–ether (1—2% of ether) eluted an intractable gum (203 mg.). Material eluted with benzene–ether (5—10%) afforded, after crystallisation from light petroleum, 5-*oxo*-3 : 5-seco-A-*norergost*-22-*en*-3-*oic acid* (295 mg.), m. p. 141—143°, $[\alpha]_D$ −4° (*c* 1·0) (Found: C, 78·2; H, 10·8. $C_{27}H_{44}O_3$ requires C, 77·85; H, 10·65%), $\nu_{max.}$ (in CS_2) 1706 (carbonyl) and 966 (*trans*-CH=CH–) cm.$^{-1}$.

22 : 23-*Dibromo*-5-*oxo*-3 : 5-seco-A-*norergostan*-3-*oic Acid*.—This was obtained by a similar reaction in which the debromination procedure was omitted. It had m. p. 196—199°, $[\alpha]_D$ +11° (*c* 1·2) (Found: C, 56·6; H, 7·9; Br, 27·5. $C_{27}H_{44}O_3Br_2$ requires C, 56·3; H, 7·7; Br, 27·7%).

De-A-*ergost*-22-*en*-5-*one* (XIII, i).—The sodium salt of 5-oxo-3 : 5-*seco*-A-norergost-22-en-3-oic acid was prepared by titrating a solution of the acid in methanol with methanolic 0·5N-sodium methoxide to phenolphthalein. One drop of very dilute hydrochloric acid was added and solvent removed, to furnish the sodium salt, which was thoroughly dried. The salt (780 mg.) and sodium phenylacetate (3·6 g.) were heated at 295—300°/0·02—0·05 mm. for 3 hr. The semi-crystalline distillate (638 mg.) was chromatographed on alumina (200 g.). Light petroleum–benzene (10 : 3) eluted material, m. p. 95—103°, which, after two crystallisations from methanol, afforded *de*-A-*ergost*-22-*en*-5-*one* (404 mg.), m. p. 101—103°, $[\alpha]_D$ −30° (*c* 1·4) (Found: C, 83·4; H, 11·7. $C_{24}H_{40}O$ requires C, 83·65; H, 11·7%), $\nu_{max.}$ (in CS_2) 1715 (carbonyl) cm.$^{-1}$.

9α-*Lumista*-4 : 6 : 22-*trien*-3-*one* (Xd).—A solution of 9α-lumista-5 : 7 : 22-trien-3β-ol (pyrocalciferol) (9·5 g.) in xylene (200 c.c.) and *cyclo*hexanone (100 c.c.) was dried by azeotropic distillation. Aluminium *iso*propoxide (7 g.) in dry xylene was added to the boiling solution and distillation was continued for 15 min. The solution was then refluxed for 40 min.; acetic acid (200 c.c.) and tetralin (500 c.c.) were added and solvents removed at 140°/17 mm. and finally at 140°/0·01 mm. More tetralin (50 c.c.) was again added and the solvent removed. The residue was taken up in dilute hydrochloric acid and ether, and the ethereal layer was worked up to yield an oil which was dissolved in chloroform (200 c.c.) and treated with a 50% w/v solution (4 c.c.) of hydrogen bromide in acetic acid for 45 min. at 20°. Pyridine was added and solvent was removed under reduced pressure. The residue in light petroleum was chromatographed on deactivated alumina (250 g.). Material eluted with light petroleum–benzene (10 : 1 ⟶ 2 : 1) crystallised from methanol, to give 9α-*lumista*-4 : 6 : 22-*trien*-3-*one* (3·56 g.), m. p. 87—91°, $[\alpha]_D$ +68° (*c* 1·0) (Found: C, 85·4; H, 10·9. $C_{28}H_{42}O$ requires C, 85·2; H, 10·75%), $\lambda_{max.}$ 2880 Å (ε 24,000), $\nu_{max.}$ (Nujol mull) 1667 (doubly conjugated carbonyl), 1613 and 1582 (conjugated double bonds), and 970 (*trans*-CH=CH–) cm.$^{-1}$. [Note: it was not possible to obtain crystalline 9α-lumista-4 : 7 : 22-trien-3-one; the crude product of Oppenauer oxidation was therefore directly isomerised.]

9α-*Lumista*-4 : 22-*dien*-3-*one* (cf. ref. 13) (XId).—The above trienone (3·32 g.) in ethanol (150 c.c.) containing potassium hydroxide (15 mg.) was hydrogenated in the presence of 5% palladium–norite (750 mg.) until 1·03 mol. of hydrogen had been absorbed. Acetic acid (0·1 c.c.) and pyridine (0·1 c.c.) were added, the catalyst was filtered off, and the solvent removed under reduced pressure. A sample (70 mg.) of the crude product was chromatographed on deactivated alumina (5 g.). Elution with light petroleum–benzene (2 : 1) afforded material which crystallised from ethanol to give 9α-*lumista*-4 : 22-*dien*-3-*one* (30 mg.), m. p. 140—143°, $[\alpha]_D$ −53° (*c* 0·9) (Found: C, 84·4; H, 11·0. $C_{28}H_{44}O$ requires C, 84·8; H, 11·2%), $\lambda_{max.}$ 2420 Å (ε 14,900).

22 : 23-*Dibromo*-9α-*lumist*-4-*en*-3-*one*.—The remainder of the above crude product (3·15 g.) in chloroform (700 c.c.; alcohol-free) was cooled to −80° and a 2% v/v solution of bromine in chloroform (27·5 c.c.) added dropwise with stirring. Triethylamine (0·5 c.c.) was added, solvent

removed under reduced pressure, and the residue, in light petroleum–benzene (50 : 1), chromatographed on silica gel (275 g.). Material eluted with benzene and benzene–ether (100 : 1) crystallised from ethanol, to give 22 : 23-*dibromo*-9α-*lumist*-4-*en*-3-*one* (1·89 g.), m. p. 190—192°, $[\alpha]_D$ −37° (*c* 1·2) (Found: C, 60·1; H, 7·8. $C_{28}H_{44}OBr_2$ requires C, 60·45; H, 7·95%), $\lambda_{max.}$ 2410 Å (ε 15,000).

5-*Oxo*-3 : 5-seco-A-*nor*-9α-*lumist*-22-*en*-3-*oic Acid* (XIId).—A solution of 22 : 23-dibromo-9α-lumist-4-en-3-one (1·79 g.) in " AnalaR " ethyl acetate (150 c.c.) was ozonised and treated with acetic acid and hydrogen peroxide, and after 40 hr., isolation *via* ether gave an oil which was treated with activated zinc dust (2 g.) in ether–methanol, as above. The semi-crystalline product was taken up in dilute hydrochloric acid and ether. The ethereal layer was extracted with 2N-sodium hydroxide, and the alkaline washings were acidified with 2N-hydrochloric acid, to furnish, after isolation with ether and crystallisation from ethanol, 5-*oxo*-3 : 5-seco-A-*nor*-9α-*lumist*-22-*en*-3-*oic acid* (513 mg.), m. p. 190—197°, $[\alpha]_D$ −43·5° (*c* 1·1) (Found: C, 77·55; H, 10·6. $C_{27}H_{44}O_3$ requires C, 77·85; H, 10·65%).

Tricyclic Ketone from 9α-*Lumisterol.*—Aqueous 0·061N-barium hydroxide (9 c.c.) was added dropwise to the above acid (226 mg.) in dioxan (6 c.c.). Solvent was removed under reduced pressure and the residue dried and then heated at 300—350°/0·001 mm. The sublimate (149 mg.) in light petroleum, was chromatographed on alumina (13 g.). Material eluted with light petroleum–benzene (5 : 1 ⟶ 10 : 3) crystallised from methanol, to give the *ketone* (19 mg.), m. p. 85·5—87°, $[\alpha]_D$ +51·5° (*c* 0·9) (Found: C, 83·6; H, 11·6. $C_{24}H_{40}O$ requires C, 83·65; H, 11·7%), $\nu_{max.}$ (in CS_2) 1715 (carbonyl) and 967 (*trans*-CH=CH–) cm.$^{-1}$. The m. p. of the above ketone was strongly depressed on admixture with de-A-ergost-22-en-5-one.

Lumista-4 : 6 : 22-*trien*-3-*one* (Xc).—A 50% w/v solution (9 c.c.) of hydrogen bromide in acetic acid was added to lumista-4 : 7 : 22-trien-3-one [20] (8·8 g.) in chloroform (700 c.c.; alcohol-free). The reaction was stopped after 40 min. by addition of pyridine; solvent was removed under reduced pressure, and the oily residue taken up in light petroleum and filtered. The filtrate was reduced to small volume and adsorbed on deactivated alumina (400 g.). Next morning, when unchanged lumisterone was transformed into non-elutable material, elution with light petroleum–benzene (2 : 1) afforded material (1·7 g.) which, after two crystallisations from acetone, had m. p. 177·5—180·5°, $\lambda_{max.}$ 2490 Å [ε (*M*, 394·6) 21,300], $\nu_{max.}$ (Nujol mull) 1712 (carbonyl) cm.$^{-1}$. This unconjugated ketone was not investigated further.

Elution with light petroleum–benzene (2 : 1) and crystallisation from acetone–methanol yielded *lumista*-4 : 6 : 22-*trien*-3-*one* (3·4 g.), m. p. 99—101°, $[\alpha]_D$ −629° (*c* 1·2) (Found: C, 84·95; H, 10·6. $C_{28}H_{42}O$ requires C, 85·2; H, 10·75%), $\lambda_{max.}$ 2870 Å (ε 25,100), $\nu_{max.}$ (Nujol mull) 1660 (doubly conjugated carbonyl), 1624 and 1588 (conjugated double bonds) and 973 (*trans*-CH=CH–) cm.$^{-1}$.

Lumista-4 : 22-*dien*-3-*one* (XIc) (cf. ref. 13).—The above trienone (4·8 g.) in ethanol (250 c.c.) containing potassium hydroxide (22 mg.) was hydrogenated in the presence of 5% palladium–norite (760 mg.) until 1·1 mol. of hydrogen had been absorbed (the ratio $\varepsilon_{2430} : \varepsilon_{2860}$ was then 36). Acetic acid (1 drop) and pyridine (1 drop) were added, the catalyst was removed, and the solvent evaporated under reduced pressure. The residue in light petroleum–benzene (20 : 1) was adsorbed on deactivated alumina (200 g.). Elution with light petroleum–benzene (10 : 1) gave material (930 mg.) (probably lumist-22-en-3-one) with no intense ultraviolet absorption. Further elution with the same mixture and with light petroleum–benzene (5 : 1) gave, after crystallisation from ethanol, *lumista*-4 : 22-*dien*-3-*one* (3·5 g.), m. p. 124—125·5°, $[\alpha]_D$ −170° (*c* 1·05) (Found: C, 84·9; H, 11·3. $C_{28}H_{44}O$ requires C, 84·8; H, 11·2%), $\lambda_{max.}$ 2420 Å (ε 16,700), $\nu_{max.}$ (Nujol mull) 1675 (conjugated carbonyl), 1623 (conjugated double bond) and 983 (*trans*-CH=CH–) cm.$^{-1}$.

22 : 23-*Dibromolumist*-4-*en*-3-*one*.—A solution of lumista-4 : 22-dien-3-one (4·01 g.) in chloroform (800 c.c.; alcohol-free) was cooled to −80° and 2% v/v bromine–chloroform (28 c.c.) was added dropwise with stirring. Triethylamine was added, solvent was removed under reduced pressure, and the residue taken up in ether and filtered; removal of the ether and crystallisation from acetone–methanol furnished 22 : 23-*dibromolumist*-4-*en*-3-*one* (4·3 g.), m. p. 169—172°, $[\alpha]_D$ −102° (*c* 0·8) (Found: C, 60·2; H, 7·9. $C_{28}H_{44}OBr_2$ requires C, 60·45; H, 7·95%), $\lambda_{max.}$ 2410 Å (ε 15,900), $\nu_{max.}$ (Nujol mull) 1681 (conjugated carbonyl) and 1618 (conjugated double bond), no peak at *ca.* 970 (*trans*-CH=CH–) cm.$^{-1}$. Debromination with activated zinc dust gave,

[20] Prepared in 45% yield by using the procedure of Shepherd *et al.*[13]; the constants agreed with those given by Heilbron, Kennedy, Spring, and Swain, *J.*, 1938, 869.

in high yield, the parent lumista-4 : 22-dien-3-one, m. p. and mixed m. p. 122—125°, with light absorption properties identical with those quoted above.

22 : 23-*Dibromo*-5-*oxo*-3 : 5-seco-A-*nor*-*lumistan*-3-*oic Acid*.—A solution of 22 : 23-dibromolumist-4-en-3-one (3·95 g.) in ethyl acetate (385 c.c.) was ozonised and treated with hydrogen peroxide as above. The mixture was rapidly stirred until the initial white precipitate had dissolved (41 hr.). The solution was extracted with ether, and the ethereal layer washed with water and extracted with 2N-sodium hydroxide. Acidification of the aqueous layer with 2N-hydrochloric acid and ether-extraction furnished, after drying and removal of solvent, an oil (3·78 g.) which yielded crystals from acetone–light petroleum of 22 : 23-*dibromo*-5-*oxo*-3 : 5-seco-A-*nor*-*lumistan*-3-*oic acid* (1·32 g.), m. p. 177·5—179°, $[\alpha]_D$ +6° (*c* 1·1) (Found: C, 56·4; H, 7·6; Br, 27·5. $C_{27}H_{44}O_3Br_2$ requires C, 56·3; H, 7·7; Br, 27·7%), $\nu_{max.}$ (Nujol mull) 1715 (carbonyl) cm.$^{-1}$.

De-A-*lumist*-22-*en*-5-*one* (XIII, ii).—The above acid (1·26 g.) was treated with activated zinc dust (2·5 g.) in refluxing 1 : 1 ether–methanol (120 c.c.) for 2 hr. More zinc dust (1 g.) was added and refluxing was continued for 1 hr. The usual working up furnished an oil which from light petroleum gave 5-oxo-3 : 5-*seco*-A-norlumist-22-en-3-oic acid (800 mg.), m. p. 78—80°, $[\alpha]_D$ −11° (*c* 0·9) (no satisfactory analyses were obtained; the methyl ester was an oil), $\nu_{max.}$ (in CS_2) 1712 (carbonyl) and 967 (*trans*-CH=CH–) cm.$^{-1}$.

The sodium salt (600 mg.) of the above acid was heated with sodium phenylacetate (3 g.) at 290—300°/0·05 mm. for 3¼ hr. The oily distillate (435 mg.) was chromatographed on alumina (120 g.). Light petroleum–benzene (10 : 1 ⟶ 20 : 3) eluted *de*-A-*lumist*-22-*en*-5-*one* (355 mg.), m. p. 28—34°, $[\alpha]_D$ −48° (*c* 0·96) (Found: C, 83·8; H, 11·65. $C_{24}H_{40}O$ requires C, 83·65; H, 11·7%), $\nu_{max.}$ (in CS_2) 1715 (carbonyl) and 968 (*trans*-CH=CH–) cm.$^{-1}$.

The ketone was wax-like and could not be crystallised by conventional methods but when pure it solidified spontaneously and had the m. p. recorded above. It was recovered unchanged after treatment with 0·2N-sodium methoxide in refluxing methanol and with toluene-*p*-sulphonic acid (0·5%) in acetic acid–benzene (1 : 1) at room temperature. The *oxime* had m. p. 134·5—137°, $[\alpha]_D$ −94° (*c* 0·7) (Found: C, 80·4; H, 11·2; N, 4·1. $C_{24}H_{41}ON$ requires C, 80·2; H, 11·5; N, 3·9%).

9β-*Ergosta*-4 : 7 : 22-*trien*-3-*one* * (IXb).—A solution of 9β-ergosterol (*iso*pyrocalciferol) (41 g.) in toluene (900 c.c.) and *cyclo*hexanone (165 c.c.) was dried by azeotropic distillation in the dark. Aluminium *iso*propoxide (25 g.) in dry distillate (140 c.c.) was added and the solution refluxed for 5 hr. under nitrogen. The solution was then cooled and poured into dilute hydrochloric acid containing ice. Material isolated with ether was dried under reduced pressure and chromatographed on deactivated alumina (1 kg.). Light petroleum eluted oily condensation products (25·4 g.). Further elution with light petroleum and light petroleum–benzene (10 : 1 ⟶ 5 : 1) afforded an oil (9·7 g.) (A). Light petroleum–benzene (5 : 1 ⟶ 1 : 1) eluted semi-crystalline material (7·6 g.) (B). Material (A) was chromatographed on deactivated alumina (1 kg.). Light petroleum–benzene (10 : 1 ⟶ 5 : 1) eluted material which crystallised from methanol, to give 9β-ergosta-5 : 7 : 22-trien-3-one (XIV) (273 mg.), m. p. 123—131°, $[\alpha]_D$ +521° (*c* 0·9), $\lambda_{max.}$ 2720 (ε 9400), 2820 Å (ε 10,000), $\nu_{max.}$ (Nujol mull) 1712 (carbonyl) cm.$^{-1}$. Elution with light petroleum–benzene (5 : 1 ⟶ 10 : 3) yielded semi-crystalline material (6·2 g.) which was combined with (B) and crystallised from methanol, to give 9β-*ergosta*-4 : 7 : 22-*trien*-3-*one* (10·3 g.), m. p. 110—112·5°, $[\alpha]_D$ +185° (*c* 1·3) (Found: C, 85·4; H, 10·8. $C_{28}H_{42}O$ requires C, 85·2; H, 10·75%), $\lambda_{max.}$ 2420 Å (ε 14,200), $\nu_{max.}$ (Nujol mull) 1667 (conjugated carbonyl), 1626 (conjugated double bond) and 970 (*trans*-CH=CH–) cm.$^{-1}$.

9β-*Ergosta*-4 : 6 : 22-*trien*-3-*one* (cf. ref. 13) (Xb).—Concentrated hydrochloric acid (2 c.c.) was added to 9β-ergosta-4 : 7 : 22-trien-3-one (1·033 g.) in methanol (40 c.c.), and the solution refluxed for 45 min., then cooled, diluted with ether, and treated with excess of solid sodium hydrogen carbonate. The mixture was filtered, the solid being washed with ether. Material isolated from the filtrate was chromatographed on deactivated alumina (150 g.). Light petroleum–benzene (20 : 1 ⟶ 10 : 1) eluted semi-crystalline material (549 mg.) from which no homogeneous compound was obtained; repeated crystallisation from acetone–methanol afforded a solid, m. p. 105—117°, $\lambda_{max.}$ 2540 Å [ε (*M*, 394·6) 19,300], $\nu_{max.}$ (Nujol mull) 1712 (carbonyl) cm.$^{-1}$. This ketone was not investigated further.

Elution with light petroleum–benzene (5 : 1 ⟶ 10 : 3) afforded a solid which crystallised

* The original experimental work on this oxidation was carried out by Miss S. Ridley, Ph.D. Thesis, Manchester 1955.

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from acetone–methanol to give 9β-*ergosta*-4 : 6 : 22-*trien*-3-*one* (280 mg.), m. p. 161—164°, $[\alpha]_D$ −14° (*c* 0·98) (Found: C, 85·5; H, 10·65. $C_{28}H_{42}O$ requires C, 85·2; H, 10·75%), $\lambda_{max.}$ 2840 Å (ε 26,200), $\nu_{max.}$ (Nujol mull) 1656 (doubly conjugated carbonyl), 1623 and 1587 (conjugated double bonds), and 965 (*trans*-CH=CH–) cm.$^{-1}$.

9β-*Ergosta*-4 : 22-*dien*-3-*one* (XIb).—9β-Ergosta-4 : 6 : 22-trien-3-one (2·4 g.) in ethanol (370 c.c.) containing potassium hydroxide (11 mg.) was hydrogenated in the presence of 5% palladium–norite (380 mg.) until 1·1 mol. of hydrogen had been absorbed. Acetic acid (2 drops) and pyridine (2 drops) were added, the catalyst was removed, and solvent evaporated under reduced pressure. The residue (which had a ratio $\varepsilon_{2440} : \varepsilon_{2860} = 11$) was chromatographed on deactivated alumina (130 g.). Light petroleum–benzene (20 : 1 ⟶ 20 : 3) eluted material (377 mg.) (probably 9β-ergost-22-en-3-one) with no intense ultraviolet absorption. Elution with light petroleum–benzene (20 : 3 ⟶ 2 : 1) afforded a product which after two crystallisations from acetone–methanol gave 9β-*ergosta*-4 : 22-*dien*-3-*one* (1·54 g.), m. p. 155—157°, $[\alpha]_D$ +25° (*c* 1·0) (Found: C, 85·0; H, 11·1. $C_{28}H_{44}O$ requires C, 84·8; H, 11·2%), $\lambda_{max.}$ 2440 Å (ε 14,500), $\nu_{max.}$ (Nujol mull) 1667 (conjugated carbonyl), 1616 (conjugated double bond) and 965 (*trans*-CH=CH–) cm.$^{-1}$.

22 : 23-*Dibromo*-9β-*ergost*-4-*en*-3-*one*.—A solution of 9β-ergosta-4 : 22-dien-3-one (1·41 g.) in chloroform (300 c.c.; alcohol-free) was cooled to −80° and bromine in chloroform (9·8 c.c.; 2% v/v) was added dropwise with stirring. Triethylamine was added, solvent removed under reduced pressure, and the residue dissolved in ether and filtered. Removal of the ether and crystallisation of the residue from acetone–ethanol afforded 22 : 23-*dibromo*-9β-*ergost*-4-*en*-3-*one* (1·4 g.), m. p. 203·5—206°, $[\alpha]_D$ +39° (*c* 0·9) (Found: C, 60·6; H, 7·8; Br, 28·3. $C_{28}H_{44}OBr_2$ requires C, 60·45; H, 7·95; Br, 28·7%), $\lambda_{max.}$ 2440 Å (ε 16,700), $\nu_{max.}$ (Nujol mull) 1669 (conjugated carbonyl) and 1621 (conjugated double bond), no peak at *ca.* 970 (*trans*-CH=CH–) cm.$^{-1}$. Debromination with activated zinc dust gave a high yield of the parent 9β-ergosta-4 : 22-dien-3-one, m. p. and mixed m. p. 155—157°, $[\alpha]_D$ +25° (*c* 1·0), $\lambda_{max.}$ 2440 Å (ε 14,500).

22 : 23-*Dibromo*-5-*oxo*-3 : 5-seco-A-*nor*-9β-*ergostan*-3-*oic Acid*.—22 : 23-Dibromo-9β-ergost-4-en-3-one (1·15 g.) in ethyl acetate (300 c.c.) was ozonised as above. Isolation of the acid as before gave semi-solid material which crystallised from acetone–light petroleum, affording 22 : 23-*dibromo*-5-*oxo*-3 : 5-seco-A-*nor*-9β-*ergostan*-3-*oic acid* (760 mg.), m. p. 178—182°, $[\alpha]_D$ −9° (*c* 0·95) (Found: C, 56·65; H, 7·45; Br, 27·9. $C_{27}H_{44}O_3Br_2$ requires C, 56·3; H, 7·7; Br, 27·7%), $\nu_{max.}$ (in CS_2) 1712 (carbonyl) cm.$^{-1}$.

Des-A-*lumist*-22-*en*-5-*one* (XIII, ii) *from the Acid of the* 9β-*Ergosterol Series*.—The above acid (690 mg.) was treated with activated zinc dust (1·3 g.) in refluxing 1 : 1 ether–methanol (64 c.c.) for 2 hr. More zinc dust (530 mg.) was added and refluxing was continued for 1 hr. The usual working up afforded a solid (480 mg.) which readily formed gels with a variety of solvents and was not obtained crystalline. The gel formed from light petroleum was cooled to −80°, filtered, and dried under reduced pressure, to give 5-*oxo*-3 : 5-seco-A-*nor*-9β-*ergost*-22-*en*-3-*oic acid* as an amorphous solid, m. p. 92—98°, $[\alpha]_D$ −39° (*c* 1·0), $\nu_{max.}$ (in CS_2) 1712 (carbonyl) and 967 (*trans*-CH=CH–) cm.$^{-1}$. (No satisfactory analysis could be obtained.)

The sodium salt (395 mg.) of the above acid, and sodium phenylacetate (1·2 g.), were heated at 290—295°/0·02—0·05 mm. for 2½ hr. The oily distillate (257 mg.), $[\alpha]_D$ −44° (*c* 0·8), was chromatographed on alumina (50 g.). Light petroleum–benzene (4 : 1 ⟶ 2 : 1) eluted an oil (225 mg.) which solidified slowly, then having m. p. (alone or mixed with de-A-lumist-22-en-5-one) 28—34°, $[\alpha]_D$ −48° (*c* 1·0) (Found: C, 83·35; H, 11·4. Calc. for $C_{24}H_{40}O$: C, 83·65; H, 11·7%), $\nu_{max.}$ (in CS_2) 1715 (carbonyl) and 968 (trisubstituted double bond) cm.$^{-1}$. The oxime had m. p. (alone or mixed with de-A-lumist-22-en-5-one oxime) 134—137°, $[\alpha]_D$ −96° (*c* 0·85).

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The University, Manchester 13.
The Dyson Perrins Laboratory, Oxford University. [*Received, October* 23*rd*, 1958.]

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230. *Purines, Pyrimidines, and Glyoxalines. Part XII.* Some Oxaloacetic Acid Derivatives as Precursors of Orotic Acids and Related Carboxymethylenehydantoins, and a New Synthesis of 6-Methyluracils.*

By R. K. Ralph, G. Shaw, and (in part) R. N. Naylor.

cis- and *trans*-5-Carboxymethylene-1-phenylhydantoins, and *trans*-β-carboxy-β-methoxy(or chloro)acryloyl-ureas and -thioureas, have been prepared as possible precursors of orotic acids. Some reactions of these compounds are described. A new unambiguous synthesis of 1-substituted 6-methyluracils from acetoacetylurethane and primary amines is described and the oxidation of some of these compounds is discussed.

Orotic acid (IIa; R = R′ = R″ = H) and its 3-alkyl or 3-aryl derivatives † have been synthesised by base-catalysed rearrangement of 5-carboxymethylenehydantoin [1] (I; R = R′ = R″ = H, X = O) or its corresponding 3-substituted derivatives,[2] by the oxidation of 6-methyluracil (III; R = R′ = H) by alkaline potassium ferricyanide [3] or of 6-formyl-2-thiouracil by hydrogen peroxide and chromic oxide.[4] A synthesis of the biochemically important orotic acid glycosides related to and including orotidine [1-β-D-ribofuranosyl orotic acid (IIa; R = R″ = H, R′ = β-D-ribofuranosyl)] requires a method for the synthesis of 1-substituted orotic acids which could be used for the introduction of a glycosyl residue at $N_{(1)}$. 1-Methylorotic acid (IIa; R′ = Me, R = R″ = H) was prepared by oxidation of 1 : 6-dimethyluracil (III; R = Me, R′ = H) with alkaline ferricyanide,[5] an adaptation of the method used by Behrend and Struve [3] for oxidation of 6-methyluracil to orotic acid. 1-Substituted 6-methyluracils have hitherto been prepared only by vigorous alkylation of 6-methyluracil, an ambiguous method which leads to mixtures of 1- and 3-substituted pyrimidines.[6] 1 : 6-Dimethyluracil was also obtained unexpectedly from *N*-methylthiourea and diketen; [7] with other *N*-substituted ureas this reaction leads to 3-substituted uracils.

These methods appear to be unsuitable for the introduction of a glycosyl residue and in addition Fox, Yung, and Wempen [5] suggested that steric factors would hinder direct glycosylation at position 1 in orotic acid. In preliminary experiments we could find no evidence of condensation between metal derivatives of ethyl orotate and 2 : 3 : 5-tri-*O*-benzoylribosyl chloride.

We now report a preliminary examination of some possible synthetical routes to orotic acids which might be suitable for the introduction of glycosyl residues at position 1.

The ready rearrangement of 5-carboxymethylenehydantoin or its 3-substituted derivatives to orotic acids [1,2] suggested that the hitherto unknown 1-substituted carboxymethylenehydantoins might similarly give rise to 1-substituted orotic acids.

Ethyl acetylenedicarboxylate reacted vigorously with dithiourethane with loss of ethanol. Of the several structures possible for the product, the thiazoline structure (IV) is assigned for the following reasons. With aniline the compound liberated ethanethiol, and the product is regarded as the 1-phenylthiohydantoin (Ib; R = Et, R′ = Ph,

* Part XI, *J.*, 1959, 50.

† In this paper, as in others of this Series, the " pyrimidine " numbering of orotic acid is used.

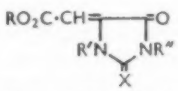
[1] Mitchell and Nyc, *J. Amer. Chem. Soc.*, 1947, **69**, 674, 1382.
[2] Atkinson, Maguire, Ralph, Shaw, and Warrener, *J.*, 1957, 2363.
[3] Behrend and Struve, *Annalen*, 1911, **378**, 153.
[4] Johnson and Schroeder, *J. Amer. Chem. Soc.*, 1931, **53**, 1989; Heidelberger and Hurlbert, *ibid.*, 1950, **72**, 4704.
[5] Fox, Yung, and Wempen, *Biochim. Biophys. Acta*, 1957, **23**, 295.
[6] Behrend and Buckendorff, *Annalen*, 1911, **385**, 314; Behrend and Thurm, *ibid.*, 1902, **323**, 160; Behrend and Hartel, *ibid.*, 1921, **422**, 83.
[7] Lacey, *J.*, 1954, 839.

R″ = H) rather than the isomeric anilinothiazoline since it was immediately soluble in dilute alkali and was stable to heat, and its ultraviolet absorption spectrum and that of the corresponding acid (Ib; R = R″ = H, R′ = Ph) derived from it by hydrolysis were very similar to that of the 3-phenylthiohydantoin (Ib; R = Et, R′ = H, R″ = Ph) which was prepared by the reaction of ethyl oxaloacetate and phenylthiourea. Alternative structures for the thiazoline would have given rise with aniline to either the 3-phenylthiohydantoin or to derivatives of thio-orotic acid.

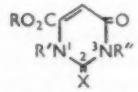
Whereas the compound (Ib; R = Et, R′ = H, R″ = Ph) behaved like its oxygen analogue and was readily converted into 3-phenyl-2-thio-orotic acid (IIb; R = R′ = H, R″ = Ph) when treated with dilute sodium hydroxide solution, as indicated by a characteristic change in its ultraviolet absorption spectrum to that of a thiouracil, the 1-phenyl derivative (Ib; R = Et, R′ = Ph, R″ = H) gave only the corresponding acid (Ib; R = R″ = H, R′ = Ph). Attempts to convert the thio-compound (Ib; R = Et, R′ = Ph, R″ = H) into the oxygen analogue by conventional methods of oxidation were unsuccessful. With ethyl iodide an ethyl derivative, presumably (V; R = Et), was obtained but hydrolysis of this with hydrogen bromide in acetic acid gave only the acid (V; R = H) and decomposition products.

The required *trans*-5-ethoxycarbonylmethylene-1-phenylhydantoin (Ia; R = Et, R′ = Ph, R″ = H) was eventually obtained by reaction of diethyl anilinofumarate (VI), prepared from aniline and ethyl oxaloacetate,[8] with the sodium derivative of urethane. The structure of the hydantoin was confirmed by a characteristic ultraviolet absorption spectrum [2] and by comparison with the *cis*-isomer described below. Hydrolysis of the ester (Ia; R = Et, R′ = Ph, R″ = H) with sodium hydroxide gave the acid (Ia; R = R″ = H, R′ = Ph) but this failed to rearrange to the related orotic acid under a variety of conditions. The amide (VII), prepared from (Ia; R = Et, R′ = Ph, R″ = H) and methanolic ammonia, equally resisted rearrangement. Further confirmation of the hydantoin structure (Ia; R = R″ = H, R′ = Ph) came from its decarboxylation when heated in quinoline containing a trace of copper powder, the methylenehydantoin (VIII; R = H) being obtained whereas a pyrimidine would have given the known 1-phenyluracil.

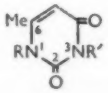
The failure of the above 1-phenylhydantoins to rearrange to orotic acids under the conditions tried prompted us to examine the preparation of possible precursors of orotic acid analogous to compounds successfully used as precursors of uracils and thiouracils,



(I) a: trans, X = O
b: X = S
c: cis, X = O



(II) a: X = O
b: X = S



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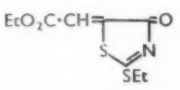

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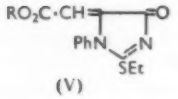
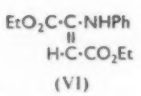
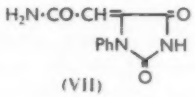


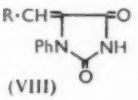
(V)



(VI)



(VII)



(VIII)

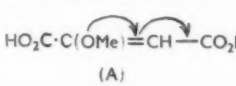
and described in other Parts of this series.[9] These compounds include β-alkoxyacryloyl *iso*cyanates and *iso*thiocyanates and derived acylurethanes and ureas, and have been used for the introduction of glycosyl radicals into uracils and thiouracils. Intermediates of this type required for the preparation of orotic acids would include β-oxaloacetyl-ureas and -thioureas (IX; R′ = H) and corresponding *O*-alkyl derivatives.

One route to the latter series required initially an alkoxy-fumaric or -maleic acid.

[8] Wislicenus and Spiro, *Ber.*, 1889, **22**, 3348.
[9] Shaw, *J.*, 1955, 1834; Shaw and Warrener, *J.*, 1958, 153, 157, 2294.

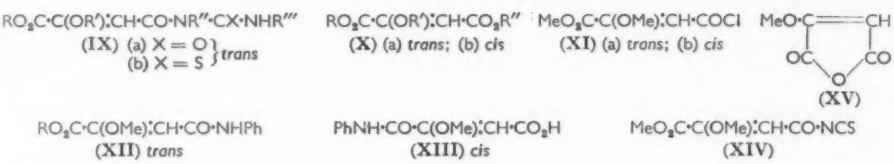
Ethoxyfumaric acid (Xa; R = R″ = H, R′ = Et) has been prepared by the reaction of ethyl *meso*-dibromosuccinate with sodium ethoxide,[10] from ethyl oxaloacetate and ethyl iodide in the presence of silver oxide,[11] and from ethyl acetylenedicarboxylate and sodium ethoxide.[12] In our hands none of these methods proved satisfactory, but an excellent yield of diethyl methoxyfumarate (Xa; R = R″ = Et, R′ = Me) was readily obtained by reaction of ethyl oxaloacetate with diazomethane. Hydrolysis of the ester gave methoxyfumaric acid (Xa; R = R″ = H, R′ = Me), the *trans*-configuration of which followed from its method of preparation and from comparison with the *cis*-isomer which was isolated in a subsequent reaction.

The acid (Xa; R = R″ = H, R′ = Me) with one equivalent of potassium hydroxide gave a crystalline acid salt regarded as (Xa; R = K, R′ = Me, R″ = H) since electron-donation from the methoxy-group across the unsaturated system would tend to leave the α-carboxyl group the more acidic (cf. A), and this was confirmed by subsequent reactions.



(A)

The corresponding silver salt with methyl iodide gave the acid ester (Xa; R = R′ = Me, R″ = H), isolated as a sodium salt (Xa; R = R′ = Me, R″ = Na) which with thionyl chloride gave a mixture of the acid chloride (XIa; R = Me) and methoxy-maleic anhydride (XV). Hydrolysis of the anhydride gave the crystalline *cis*-acid (Xb; R = R″ = H, R′ = Me) which differed from the *trans*-derivative in melting point and paper chromatographic behaviour in much the same way as maleic differs from fumaric acid. The ratio of acid chloride to anhydride obtained in this reaction varied inversely with the temperature at which the mixture was distilled, suggesting that the heat-labile *trans*-chloride is converted into the *cis*-derivative (XIb) which then cyclises with loss of methyl chloride. Also complete hydrolysis of the acid chloride gave the *trans*-acid although paper chromatograms of the mother-liquors from the hydrolysis revealed the presence of a small amount of the *cis*-acid possibly due to the presence of a trace of *cis*-acid chloride (XIb).



(IX) (a) X = O, (b) X = S } *trans*; (X) (a) *trans*; (b) *cis*; (XI) (a) *trans*; (b) *cis*; (XV)

(XII) *trans*; (XIII) *cis*; (XIV)

The *trans*-chloride (XIa) with aniline readily gave the ester-anilide (XII; R = Me) which was hydrolysed to the acid-anilide (XII; R = H). A similar compound, presumably (XIII), was obtained from the anhydride and aniline; the direction of acylation suggested here would follow from the greater reactivity of the α-carbonyl group implied in the above discussion. Reaction of the *trans*-chloride (XIa) with potassium thiocyanate in aceto-nitrile gave an oil, presumably the *iso*thiocyanate (XIV), which could not be distilled without decomposition but with aniline readily gave the acylthiourea (IXb; R = R′ = Me, R″ = H, R‴ = Ph) from which the acid (IXb; R = R″ = H, R′ = Me, R‴ = Ph) was obtained by alkaline hydrolysis. Attempts to cyclise these compounds to the corresponding thio-orotic acid were unsuccessful.

Similarly, when the acid chloride (XIa) was heated in benzene solution containing a trace of sulphuric acid, with urea, methylurea, or phenylurea, the linear acylureas (IXa; R = R′ = Me, R″ = H, R‴ = H, Me, and Ph respectively) were obtained. Treatment of the urea ester (IXa; R = R′ = Me, R″ = H, R‴ = Ph) with aqueous alkali gave the

[10] Michael and Maisch, *J. prakt. Chem.*, 1892, **46**, 233; Pum, *Acad. Wissenschaft, Wien*, 1893, II*b*, **102**, 508; *Monatsh.*, 1893, **14**, 492.
[11] Nef, *Annalen*, 1893, **276**, 227; Lander, *J.*, 1903, **83**, 417.
[12] Croxall and Schneider, U.S.P. 2,535,012/1950; U.S.P. 2,571,212/1951.

acid (IXa; R = R″ = H, R′ = Me, R‴ = Ph), but further attempts to cyclise this with a variety of reagents have so far been unsuccessful. However, relatively mild treatment of the ester (IXa; R = R′ = R‴ = Me, R″ = H) with sodium hydroxide gave a mixture which included 1-methyluracil. By contrast the urea (IXa; R = R′ = Me, R″ = R‴ = H) with dilute alkali very readily afforded orotic acid. The formation of orotic acid confirmed the structures assigned to these intermediates since an α-methoxyacylurea would have given the hydantoin (I; R = R′ = R″ = H, X = O). In addition, the products from the *trans*-chloride (XIa) and phenylurea afforded a small amount of a compound, probably (IXa; R = R′ = Me, R″ = Ph, R‴ = H), which with alkali readily gave 3-phenylorotic acid (IIa; R = R′ = H, R″ = Ph).

The results suggest that in compounds of type (IX) only those structures which contain a terminal NH_2 group are able to cyclise readily. The formation of 1-methyluracil from the urea (IXa; R = R′ = R‴ = Me, R″ = H) is of special interest and indicates that decarboxylation is occurring at some intermediate aliphatic stage since orotic acids are known to resist decarboxylation *in vitro*, although they readily undergo enzymic decarboxylation.

In a similar series of reactions, chlorofumaric acid (XVI; R = R′ = H), prepared from tartaric acid and phosphorus pentachloride,[13] was converted *via* the acid potassium salt and the silver salt into the half-ester salt (XVI; R = Me, R′ = K) which with thionyl chloride gave the acid chloride (XVII). The orientation of substituents is assumed to be the same as in the compounds derived from methoxyfumaric acid. The chloride (XVII) with aniline gave the anilide (XVIII) and with phenylurea the linear acylurea (XIX). The latter product with aqueous sodium hydroxide gave the *cis*-1-phenylhydantoin (Ic; R = R″ = H, R′ = Ph); the structure assigned to this compound is confirmed by its ultraviolet absorption spectrum which was similar to that of the *trans*-form, and by decarboxylation which gave the methylenehydantoin (VIII; R = H) identical with the substance obtained by decarboxylation of the *trans*-acid. The *cis*-hydantoin is apparently formed by *cis*-addition of the terminal NH group in the acetylene (XX).

$RO_2C{\cdot}CCl{:}CH{\cdot}CO_2R'$ (XVI) *trans*

$MeO_2C{\cdot}CCl{:}CH{\cdot}COCl$ (XVII) *trans*

$MeO_2C{\cdot}CCl{:}CH{\cdot}CO{\cdot}NHPh$ (XVIII) *trans*

$MeO_2C{\cdot}CCl{:}CH{\cdot}CO{\cdot}NH{\cdot}CO{\cdot}NHPh$ (XIX) *trans*

$MeO_2C{\cdot}C{\equiv}C{\cdot}CO{\cdot}NH{\cdot}CO{\cdot}NHPh$ (XX)

Since 1-methylorotic acid was prepared by oxidation of 1 : 6-dimethyluracil with alkaline ferricyanide, we examined more general unambiguous routes to 1-substituted 6-methyluracils than those available and mentioned earlier.

Initially, β-chlorocrotonyl chloride, prepared from β-chlorocrotonic acid and thionyl chloride,[14] was treated with silver cyanate; the product, presumably β-chlorocrotonyl *iso*cyanate with aniline and methylamine gave the acylureas (XXI; R = Ph and Me respectively). The last compound (XXI; R = Me) with sodium hydroxide gave a low yield of 1 : 6-dimethyluracil, and similarly the phenyl analogue (XXI; R = Ph) gave a compound with properties expected of 6-methyl-1-phenyluracil (III; R = Ph, R′ = H), but in view of the results obtained with the chlorofumaric acid derivatives the alternative ethylidenehydantoin structure (VIII; R = Me) for this compound could not be neglected since ultraviolet absorption data for this type of compound are scanty. These doubts were resolved by the preparation of acetoacetylurethane (XXII) from diketen and urethane in acetic acid. The acylurethane reacted rapidly with ethylamine, propylamine, *cyclo*hexylamine, and aniline, giving the linear derivatives (XXIII; R = Et, Pr, C_6H_{11}, and Ph), and with methylamine giving 1 : 6-dimethyluracil directly. The linear compounds

[13] Perkin, *J.*, 1888, **53**, 695.
[14] Autenrieth, *Ber.*, 1896, **29**, 1667.

readily cyclised to 6-methyluracils (III; R = Et, Pr, C_6H_{11}, and Ph, R′ = H) when heated alone or, better, in collidine. The phenyl derivative obtained here was identical with that obtained from β-chlorocrotonic acid. In contrast to 1 : 6-dimethyluracil which is readily oxidised by ammoniacal ferricyanide to 1-methylorotamide, the compounds (III; R = Et, Pr, C_6H_{11}, and Ph) were recovered in good yield after long treatment with this oxidising agent. Other oxidising agents used so far have proved equally unsuccessful, but the method remains of potential value, and alternative methods of oxidation are being examined in an attempt to overcome the steric effect of the 1-substituent in these compounds.

$Me{\cdot}CCl{:}CH{\cdot}CO{\cdot}NH{\cdot}CO{\cdot}NHR$ (XXI) *trans*

$Me{\cdot}CO{\cdot}CH_2{\cdot}CO{\cdot}NH{\cdot}CO_2Et$ (XXII)

$Me{\cdot}C(NHR){:}CH{\cdot}CO{\cdot}NH{\cdot}CO_2Et$ (XXIII)

Experimental

5-Ethoxycarbonylmethylene-2-ethylthio-4-oxothiazole.—Diethyl acetylenedicarboxylate [15] (8·5 g.) was added to ethyl dithiocarbamate [16] (6·05 g.), a hot, homogeneous, dark solution being soon obtained. This was cooled when the temperature exceeded 60°, to give a solid. *5-Ethoxycarbonylmethylene-2-ethylthio-4-oxothiazole* (10·3 g.) separated from ethanol as yellow needles, m. p. 85° (Found: C, 44·1; H, 4·5; N, 5·7. $C_9H_{11}O_3NS_2$ requires C, 43·8; H, 4·3; N, 5·7%), $\lambda_{max.}$ 272 mμ (ε 5025) in ethanol.

5-Carboxymethylene-1-phenyl-2-thiohydantoin.—The preceding thiazole (1·23 g.) in benzene (10 ml.) was warmed with aniline (0·5 ml.). Ethanethiol was soon liberated and a solid separated. The mixture was kept at room temperature for 24 hr. and the solid collected. *5-Ethoxycarbonylmethylene-1-phenyl-2-thiohydantoin* (1·13 g.) crystallised from ethanol as yellow plates, m. p. 210° (Found: C, 56·3; H, 4·35; N, 9·95. $C_{13}H_{12}O_3N_2S$ requires C, 56·5; H, 4·35; N, 10·15%), $\lambda_{max.}$ 327 mμ (ε 17,000) in ethanol. A mixed m. p. with the 3-phenyl derivative was depressed. This thiohydantoin (0·1 g.) was heated at 100° with 1·5N-sodium hydroxide (1 ml.) for 30 min. Acidification of the cooled solution gave a solid precipitate. *5-Carboxymethylene-1-phenyl-2-thiohydantoin* (0·05 g.) separated from methanol as pale yellow needles, m. p. 300° (decomp.) (Found: C, 53·1; H, 3·05; N, 11·05. $C_{11}H_8O_3N_2S$ requires C, 53·25; H, 3·25; N, 11·3%), $\lambda_{max.}$ 323 mμ (ε 16,230) and 225 mμ (ε 16,200) in ethanol. The compound was recovered unchanged after being heated with 2N-sodium hydroxide for several hr., and was not desulphurised by alkaline hydrogen peroxide or chloroacetic acid.

5-Ethoxycarbonylmethylene-3-phenyl-2-thiohydantoin.—Dry hydrogen chloride was passed through a hot (steam-bath) solution of diethyl oxaloacetate [from the sodium salt (22 g.)] and phenylthiourea (15·2 g.) in acetic acid (24 ml.) for 30 min. The solution was set aside at 0° for 24 hr. and a crystalline precipitate collected. *5-Ethoxycarbonylmethylene-3-phenyl-2-thiohydantoin* (4 g.) recrystallised from ethanol as slender pale yellow needles, m. p. 175° (Found: C, 56·5; H, 4·35; N, 10·35. $C_{16}H_{12}O_3N_2S$ requires C, 56·5; H, 4·4; N, 10·35%), $\lambda_{max.}$ 340 mμ (ε 26,680) in ethanol.

3-Phenyl-2-thio-orotic Acid.—The last-mentioned thiohydantoin (0·1 g.) was stirred with 2N-sodium hydroxide at 20° until a clear solution was obtained. This was acidified to precipitate *3-phenyl-2-thio-orotic acid* (0·08 g.) which separated from ethanol as an ethanol *solvate*, m. p. 200° (decomp.) (Found: C, 53·45; H, 4·95; N, 8·75. $C_{11}H_8O_3N_2S,1\frac{1}{2}C_2H_6O$ requires C, 53·05; H, 5·1; N, 9·15%), or from water as a *hydrate*, m. p. 226° (decomp.) (Found: C, 48·8; H, 3·65; N, 10·25. $C_{11}H_8O_3N_2S,1\frac{1}{2}H_2O$ requires C, 48·8; H, 3·8; N, 10·35%), $\lambda_{max.}$ 275 mμ (ε 16,000) in ethanol.

5-Ethoxycarbonylmethylene-2-ethylthio-4 : 5-dihydro-4-oxo-1-phenylglyoxaline.—A solution of 5-ethoxycarbonylmethylene-1-phenyl-2-thiohydantoin (0·5 g.) in ethanol (10 ml.) containing sodium ethoxide (0·136 g.) and ethyl iodide (1 ml.) was heated under reflux for 6 hr.; the solution had by then become neutral. The solvent was evaporated and the residue with ethanol gave crystals. The *glyoxaline* (0·29 g.) separated from ethanol as yellow needles, m. p. 120° (Found: C, 58·6; H, 5·3; N, 8·9. $C_{15}H_{16}O_3N_2S$ requires C, 59·0; H, 5·25; N, 9·2%).

[15] Michael, *J. prakt. Chem.*, 1892, **46**, 224.
[16] Delépine, *Bull. Soc. chim. France*, 1903, **29**, 52.

XUM

This ester (0·33 g.) was boiled with 30% hydrogen bromide in acetic acid (2 ml.) for 1 hr. The solution was evaporated *in vacuo* and the residue dissolved in N-sodium hydroxide, and the filtered solution acidified to precipitate the *glyoxaline-acid* (0·22 g.) which separated from ethanol as needles, m. p. 200° (decomp.) (Found: C, 56·8; H, 4·5; N, 10·0. $C_{13}H_{12}O_3N_2S$ requires C, 56·8; H, 4·4; N, 10·15%).

trans-5-*Ethoxycarbonylmethylene*-1-*phenylhydantoin*.—Diethyl anilinofumarate [8] (7·9 g.) was added to a suspension of sodium urethane (3·35 g.) in ether (40 ml.). The mixture was warmed, rapidly darkening while the solid dissolved. After 10 min. the solution was added to water (10 ml.), and the ether evaporated to leave a solid. The *sodium salt* of the hydantoin separated from ethanol as a *dihydrate* which formed needles, m. p. 126° (Found: C, 48·55; H, 4·9; N, 8·7. $C_{13}H_{11}O_4N_2Na,2H_2O$ requires C, 49·05; H, 4·7; N, 8·8%). The salt (0·626 g.) was stirred with 2N-hydrochloric acid (5 ml.), and the resulting solid collected; trans-5-*ethoxycarbonylmethylene*-1-*phenylhydantoin* (0·5 g.) recrystallised from water as needles, m. p. 167° (Found: C, 60·05; H, 5·6; N, 10·85. $C_{13}H_{12}O_4N_2$ requires C, 60·0; H, 4·6; N, 10·75%), $\lambda_{max.}$ 297 (ε 6100) and 232 mμ (ε 11,350) in water.

The ester (1 g.) was heated at 100° with 2N-sodium hydroxide (5 ml.) for 30 min., and the cooled solution acidified, precipitating the *hydantoin-acid* (0·6 g.) which separated from water as hydrated prisms, m. p. 222° (decomp.) (Found: C, 52·4; H, 3·85; N, 11·3. $C_{11}H_8O_4N_2,H_2O$ requires C, 52·8; H, 3·2; N, 11·2. $C_{11}H_8O_4N_2,1\frac{1}{2}H_2O$ requires C, 52·3; H, 4·05; N, 11·1%), $\lambda_{max.}$ 308 (ε 6960) and 230 mμ (ε 11,790) in ethanol. Attempts to rearrange this compound to a pyrimidine failed. Prolonged treatment with aqueous alkali at 100° or with sodium methoxide caused decomposition.

5-*Methylene*-1-*phenylhydantoin*.—A solution of the foregoing acid (0·423 g.) in quinoline (3 ml.) containing copper powder (0·1 g.) was boiled under reflux for 1 hr. The cooled solution was extracted with N-sodium hydroxide (5 ml.), and the aqueous phase washed with ether, then acidified to precipitate 5-*methylene*-1-*phenylhydantoin* (0·023 g.) which separated from water as needles, m. p. 160° (Found: C, 63·6; H, 4·3; N, 14·65. $C_{10}H_8O_2N_2$ requires C, 63·9; H, 4·25; N, 14·9%).

trans-5-*Carbamoylmethylene*-1-*phenylhydantoin*.—The last-mentioned ester (0·164 g.) was heated in a sealed tube at 100° with saturated methanolic ammonia (5 ml.) for 1 hr. The solvent was evaporated and the residue washed with dilute hydrochloric acid. The *amide* (0·125 g.) separated from ethanol as needles, m. p. 276 (decomp.) (Found: C, 57·15; H, 4·05; N, 18·0. $C_{11}H_9O_3N_3$ requires C, 57·15; H, 3·9; N, 18·2%), $\lambda_{max.}$ 307 (ε 4650) and 235 mμ (ε 7430) in water.

Diethyl Methoxyfumarate.—Diazomethane was prepared from *N*-methyl-*N*-nitrosourea (90 g.) and 50% aqueous potassium hydroxide under ether (1300 ml.). The dried (KOH) ether solution was added to a solution of diethyl oxaloacetate (94 g.) in ether (100 ml.) at 0°. A vigorous reaction occurred and nitrogen was briskly liberated. After 30 min., excess of diazomethane was removed with acetic acid, and the solution washed with sodium hydrogen carbonate solution and water, dried, and evaporated to an oil which was distilled *in vacuo* to give *diethyl methoxyfumarate* (82 g.), b. p. 100°/0·5 mm., n_D^{25} 1·4725 (Found: C, 53·15; H, 6·75. $C_7H_{14}O_5$ requires C, 53·45; H, 7·0%). An alcoholic solution of the ester failed to give a colour with ferric chloride.

Methoxyfumaric Acid.—The ester (10 g.) was shaken with 4·08N-sodium hydroxide (25 ml.) at room temperature until a clear solution was obtained (3 hr.). This was cooled to 0° and acidified with 10N-hydrochloric acid (20 ml.), and the solution extracted with ether (6 × 20 ml.). Evaporation of the combined and dried extracts left a crystalline residue. *Methoxyfumaric acid* (5·3 g.) recrystallised from ethyl acetate–hexane as needles, m. p. 146° (Found: C, 41·0; H, 3·95%; equiv., 145·4. $C_5H_6O_5$ requires C, 41·1; H, 4·1%; equiv., 146%. On an ascending paper chromatogram, in butanol–formic acid–water (10 : 2 : 15), the acid travelled as a discrete acidic spot, R_F 0·86.

Potassium Hydrogen Methoxyfumarate.—(*a*) One half of a solution of methoxyfumaric acid (14 g.) in water (400 ml.) was neutralised to phenolphthalein with potassium hydroxide and then added to the remaining half of the solution. The solvent was removed *in vacuo* (bath 50°) to give the *potassium salt*, which crystallised from aqueous methanol as prisms (Found: C, 32·4; H, 2·8. $C_5H_5O_5K$ requires C, 32·6; H, 2·7%). (*b*) Diethyl methoxyfumarate (20·2 g.) was shaken with 3·62N-potassium hydroxide (55·25 ml.) until a clear solution of near neutrality was obtained. This was cooled to 5° and treated with acetic acid (6 ml.), to give a crystalline

precipitate; evaporation of the filtrate to 30 ml. gave a further small quantity of the salt. The potassium salt (13 g.) separated from aqueous methanol as prisms, m. p. >300° (Found: C, 32·7; H, 2·75%).

Sodium trans-β-*Methoxy*-β-*methoxycarbonylacrylate*.—The foregoing potassium salt (12·75 g.) in warm water (100 ml.) with silver nitrate (12·8 g.) in water (12 ml.) gave a solid precipitate (11·7 g.) which was collected and washed with water, ethanol, and ether, and dried *in vacuo* in the dark. A suspension of the silver salt (11·42 g.) in ether (50 ml.) containing methyl iodide (10 ml.) was boiled under reflux for 6 hr. The mixture was filtered, and the filtrate evaporated *in vacuo* to a strongly acidic oil (5·25 g.). This was suspended in water (10 ml.) and titrated to pH 8 (external indicator) with sodium hydroxide solution. The clear solution was evaporated *in vacuo* (bath <50°) and the solid residue dried over phosphoric oxide *in vacuo* and then at 100°/0·1 mm. The *sodium salt* (5·1 g.) separated from ethanol–ether as prisms, m. p. >300° (Found: C, 39·0; H, 4·05. $C_6H_7O_5Na$ requires C, 39·55; H, 3·85%).

Reaction of Sodium trans-β-*Methoxy*-β-*methoxycarbonylacrylate with Thionyl Chloride*.—(*a*) Freshly distilled thionyl chloride (20 ml.) was added to a suspension of the sodium salt (17·1 g.) in ether (50 ml.): a vigorous reaction occurred. The mixture was refluxed for 3 hr., then distilled *in vacuo* from an excess of glass wool to give trans-β-*methoxy*-β-*methoxycarbonylacryloyl chloride* (8 g.), b. p. 65°/0·1 mm. (Found: C, 41·0; H, 3·8. $C_6H_7O_4Cl$ requires C, 40·35; H, 3·9%), and *methoxymaleic anhydride* (2·1 g.), b. p. 100°/0·1 mm. (Found: C, 47·05; H, 3·2. $C_5H_4O_4$ requires C, 46·9; H, 3·15%). (*b*) In a similar reaction the sodium salt (12·3 g.) and thionyl chloride (10 ml.) gave the acid chloride (3·88 g.), b. p. 98—100°/8 mm., and the anhydride (2·16 g.), b. p. 140°/8 mm.

Methoxymaleic Acid.—The foregoing anhydride (0·5 ml.) was stirred and gently warmed with water (0·5 ml.) until a homogeneous solution was obtained. This was cooled to give a crystalline precipitate. *Methoxymaleic acid* (0·5 g.) separated from a little ethyl acetate as prisms, m. p. 126° (Found: C, 41·3; H, 4·0%; equiv., 148). The acid ran as a single acidic spot, R_F 0·57, on paper in butanol–formic acid–water (10 : 2 : 15).

Hydrolysis of trans-β-*Methoxy*-β-*methoxycarbonylacryloyl Chloride*.—A little acid chloride was treated with water, the resulting solution evaporated *in vacuo*, and the residue crystallised from ethyl acetate–hexane to give methoxyfumaric acid, m. p. and mixed m. p. 146°. The mother-liquors were chromatographed on paper with butanol–formic acid–water (10 : 2 : 15). A strongly acidic spot (R_F 0·86) corresponding to methoxyfumaric acid, and a weakly acidic spot corresponding to methoxymaleic acid (R_F 0·57), were obtained.

trans-β-*Carboxy*-β-*methoxy*-N-*phenylacrylamide*.—The above acid chloride (0·1 ml.) and aniline (0·1 ml.) were mixed, a vigorous reaction occurring. The solid residue was triturated with dilute hydrochloric acid and the solid filtered off. trans-β-*Methoxycarbonyl*-β-*methoxy*-N-*phenylacrylamide* (0·074 g.) crystallised from aqueous ethanol as plates, m. p. 106° (Found: C, 61·35; H, 5·4; N, 6·1. $C_{12}H_{13}O_4N$ requires C, 61·25; H, 5·55; N, 5·95%). The ester (0·126 g.) was warmed with N-sodium hydroxide (2 ml.) for 5 min. at 60°. The cooled solution when acidified precipitated trans-β-*carboxy*-β-*methoxy*-N-*phenylacrylamide* (0·07 g.) which separated from water as plates, m. p. 125° (Found: C, 60·0; H, 5·05; N, 6·45. $C_{11}H_{11}O_4N$ requires C, 59·75; H, 5·0; N, 6·35%).

cis-β-*Carboxy*-α-*methoxy*-N-*phenylacrylamide*.—Methoxymaleic anhydride (0·5 g.) and aniline (0·5 ml.) were mixed and the resulting solid was washed with dilute hydrochloric acid. The cis-*acid* (0·33 g.) separated from ethanol as needles, m. p. 160° (sealed tube) (Found: C, 59·55; H, 4·7; N, 6·65%).

trans-N-(β-*Methoxy*-β-*methoxycarbonylacryloyl*)-N′-*phenylthiourea*.—The above acid chloride (1·26 g.) in dry acetonitrile (10 ml.) was shaken with dry potassium thiocyanate (0·7 g.) for 1 hr. The resulting orange mixture was evaporated *in vacuo* to a gum which was stirred with dry ether (20 ml.). The mixture was filtered, and the yellow filtrate treated with aniline (0·6 g.), a vigorous exothermal reaction occurring. The cooled solution was washed with dilute hydrochloric acid, dried, and evaporated to a gum which dissolved in ethanol (2 ml.). The solution gave a crystalline precipitate after a short time. trans-N-(β-*Methoxy*-β-*methoxycarbonylacryloyl*)-N′-*phenylthiourea* (0·945 g.) separated from ethanol as prisms, m. p. 140° (Found: C, 53·3; H, 4·85; N, 9·8. $C_{13}H_{14}O_4N_2S$ requires C, 53·05; H, 4·8; N, 9·5%).

trans-N-(β-*Carboxy*-β-*methoxyacryloyl*)-N′-*phenylthiourea*.—The foregoing ester (0·62 g.) was heated with 2N-sodium hydroxide (3 ml.) for 30 min. at 100°. The cooled solution was diluted with water (2 ml.), treated with charcoal, and acidified. The precipitated trans-*acid*

(0·5 g.) crystallised from water as laths, m. p. 220° (decomp.) (Found: C, 51·35; H, 4·4; N, 9·75. $C_{12}H_{12}O_4N_2S$ requires C, 51·45; H, 4·3; N, 10·0%).

cis-N-(β-*Carboxy*-β-*methoxyacryloyl*)-N′-*phenylthiourea*.—When the last-mentioned reaction was carried out with unrecrystallised ester, the acid mother-liquors gave cis-N-(β-*carboxy*-β-*methoxyacryloyl*)-N′-*phenylthiourea* (0·02 g.) which recrystallised from water as prisms, m. p. 166° (Found: C, 51·85; H, 4·2; N, 9·8%).

The foregoing *trans*-ester was unaffected by ethanolic sodium ethoxide and was converted into the *trans*-acid by dry hydrogen chloride in acetic acid. Aqueous or aqueous-alcoholic solutions of the ester were degraded by prolonged treatment with acid, to red tars.

trans-N-(β-*Methoxy*-β-*methoxycarbonylacryloyl*)*urea*.—The above acid chloride (0·56 g.) with urea (0·26 g.) in benzene (20 ml.) containing sulphuric acid (0·01 ml.) was boiled under reflux for 4 hr. The solution was decanted from a dark insoluble gum, then cooled to give a crystalline precipitate. trans-N-(β-*methoxy*-β-*methoxycarbonylacryloyl*)*urea* (0·148 g.) separated from ethanol as needles, m. p. 100° (Found: C, 41·55; H, 5·05; N, 13·7. $C_7H_{10}O_5N_2$ requires 41·6; H, 5·0; N, 13·85%)

Orotic Acid.—The last-mentioned urea (0·25 g.) was warmed for a few min. with 2N-sodum hydroxide (3 ml.), cooled, and acidified to precipitate orotic acid (0·15 g.), m. p. and mixed m. p. 340°. The filtrate was chromatographed on paper in butanol–formic acid–water (77 : 13 : 10): only orotic acid (R_F 0·21) was detected. There was no spot corresponding to carboxymethylenehydantoin (R_F 0·56) which was chromatographed at the same time.

trans-N-(β-*Methoxy*-β-*methoxycarbonylacryloyl*)-N′-*methylurea*.—The above acid chloride (1·026 g.), methylurea (0·413 g.), sulphuric acid (0·02 ml.), and benzene (10 ml.) were boiled together under reflux for 3 hr. The solution was cooled and a crystalline precipitate collected. The trans-*methylurea* (0·35 g.) separated from ethanol as needles, m. p. 138° (Found: C, 44·4; H, 5·65; N, 13·2. $C_9H_{12}O_5N_2$ requires C, 44·45; H, 5·6; N, 12·95%). The compound gave a single absorbing spot (R_F 0·92) when chromatographed on paper in butanol–formic acid–water (77 : 13 : 10). It sublimed unchanged *in vacuo* at temperatures above the m. p., but decomposed when heated at 195° for 30 min. The compound was also recovered after treatment with hydrogen chloride in acetic acid. The urea (0·5 g.) was warmed with 2N-sodium hydroxide (5 ml.) at 50° for 5 min. The cooled solution was acidified to give a solid precipitate. This crystallised from water to give as a first crop unchanged methylurea, m. p. and mixed m. p. 136—137°; a second fraction, m. p. 175—180°, could not be obtained pure. The mother-liquors were chromatographed in butanol–formic acid–water (77 : 13 : 10): absorbing spots of R_F's 0·9, 0·6, and 0·45 were observed. The first of these corresponded to the original methylurea (R_F 0·92) and the last to 1-methyluracil (R_F 0·45). In a solvent system of propanol–hydrochloric acid–water (68 : 20 : 12) an absorbing spot corresponding to 1-methyluracil (R_F 0·88) was again observed. The original acid filtrate was extracted with ethyl acetate. Evaporation of the dried extract and recrystallisation of the residue from ethyl acetate–light petroleum (b. p. 40—60°) gave a small amount of 1-methyluracil (0·03 g.), m. p. and mixed m. p. 233—234°.

trans-N-(β-*Methoxy*-β-*methoxycarbonylacryloyl*)-N′-*phenylurea*.—The above acid chloride (2·61 g.), phenylurea (1·99 g.), sulphuric acid (0·02 ml.), and benzene (40 ml.) were boiled together under reflux for 3 hr. The solvent was removed *in vacuo*: the residual gum crystallised when triturated with ethanol. The *phenylurea* (1·28 g.) recrystallised from ethanol as needles, m. p. 130° (Found: C, 56·0; H, 4·9; N, 10·3. $C_{13}H_{14}O_5N_2$ requires C, 56·1; H, 5·05; N, 10·05%). In this reaction a small amount of crystalline material was insoluble in hot ethanol, had m. p. 234°, and was insoluble in sodium hydrogen carbonate solution. It dissolved when warmed for a few min. with 2N-sodium hydroxide. Acidification of the cooled solution precipitated 3-phenylorotic acid hydrate, m. p. and mixed m. p. 278—280° (decomp.) (Found: C, 52·95; H, 3·75; N, 11·2. Calc. for $C_{11}H_9O_4N_2,H_2O$: C, 52·8; H, 4·05; N, 11·2%).

trans-N-(β-*Carboxy*-β-*methoxyacryloyl*)-N′-*phenylurea*.—The last-mentioned ester (0·433 g.) was heated at 100° for 1 hr. with 2N-sodium hydroxide (2 ml.). The cooled solution was acidified to precipitate the phenylurea (0·4 g.) which separated from water as needles of a *hydrate*, m. p. 180° (Found: C, 51·15; H, 4·75; N, 9·8. $C_{12}H_{12}O_5N_2,\frac{1}{4}H_2O$ requires C, 51·9; H, 4·85; N, 10·1%); a sample dried at 120° for 1 hr. gave analytical figures for the anhydrous *acid* (Found: C, 54·2; H, 4·7; N, 10·55. $C_{12}H_{12}O_5N_2$ requires C, 54·5; H, 4·6; N, 10·6%). The foregoing ester was largely decomposed when treated with hydrogen bromide in acetic acid, aluminium chloride in benzene, or sodium in ammonia, and was converted into the above acid by sodium ethoxide in ethanol at 100° for 2 hr.

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trans-β-*Chloro*-β-*methoxycarbonylacryloyl Chloride*.—Half of a solution of chlorofumaric acid [13] (43 g.) in warm water (90 ml.) was neutralised with 10N-potassium hydroxide (to phenolphthalein), then mixed with the remaining solution to give a precipitate. This was collected and a further quantity of the acid *potassium salt* was obtained by evaporation of the filtrate *in vacuo*. The yield of salt, washed with ethanol and ether and dried, was 54 g. A portion of the salt separated from aqueous ethanol as prisms (Found: C, 25·6; H, 1·2. $C_4H_2O_4ClK$ requires C, 25·45; H, 1·05%). The salt (54 g.) was dissolved in water and treated with silver nitrate (50 g.) in a minimum of water, to give a solid precipitate (55 g.). The dry silver salt (55 g.), suspended in ether (250 ml.) containing methyl iodide (70 g.), was boiled under reflux for 6 hr. The mixture was filtered, and the filtrate evaporated *in vacuo* to an acidic oil. This was dissolved in ethanol and titrated with 7·15N-potassium hydroxide solution until neutral, and the solution evaporated *in vacuo* to a solid residue (18·2 g.). The dried salt (18 g.) in ether (50 ml.) containing thionyl chloride (20 g.) was refluxed for 3 hr. The solvent was removed and the residue distilled directly *in vacuo* from an excess of glass wool to give the *acid chloride* (7·5 g.), b. p. 98—100°/14 mm. (Found: Cl, 38·3. $C_5H_4O_3Cl_2$ requires Cl, 38·8%). This chloride with aniline gave trans-β-*chloro*-β-*methoxycarbonyl*-N-*phenylacrylamide*, which separated from hexane as needles m. p. 78° (Found: C, 55·2; H, 4·15; N, 5·85. $C_{11}H_{10}O_3NCl$ requires C, 55·3; H, 4·05; N, 5·95%).

trans-N-(β-*Chloro*-β-*methoxycarbonylacryloyl*)-N′-*phenylurea*.—A mixture of the acid chloride (1·475 g.) and phenylurea (1·36 g.) in benzene (20 ml.) containing sulphuric acid (0·02 ml.) was boiled under reflux for 3 hr. An upper layer was decanted from the cooled mixture and evaporated to a solid. The *phenylurea* (0·34 g.) separated from hexane as needles, m. p. 126° (Found: C, 51·0; H, 3·9; N, 9·9. $C_{12}H_{11}O_4N_2Cl$ requires C, 50·95; H, 3·9; N, 9·9%).

cis-5-*Carboxymethylene*-1-*phenylhydantoin*.—The foregoing phenylurea (0·127 g.) was heated on a water-bath for 10 min. with 2N-sodium hydroxide (1 ml.). The cooled solution was acidified to give a solid precipitate (0·075 g.) which was chlorine-free. The cis-*hydantoin* separated from water as needles, m. p. 220° (decomp.) (Found: C, 56·75; H, 3·7; N, 12·1. $C_{11}H_8O_4N_2$ requires C, 56·9; H, 3·45; N, 12·05%), $\lambda_{max.}$ 298 (ε 6280) and 230 mμ (ε 14,090) in ethanol. A mixed m. p. with the *trans*-isomer was depressed considerably. The *cis*-isomer was also obtained by reaction of the above phenylurea with ethanolic potassium acetate. The *cis*-hydantoin (0·14 g.) was decarboxylated in quinoline and worked up as for the *trans*-isomer, to give 5-methylene-1-phenylhydantoin (0·048 g.), m. p. and mixed m. p. 162°.

N-β-*Chlorocrotonoyl*-N′-*phenylurea*.—A solution of β-chlorocrotonoyl chloride [14] (2·41 g.) in benzene (20 ml.) was boiled under reflux with silver cyanate (7·1 g.) for 1 hr. The mixture was treated with aniline (2·18 g.), then filtered, and the filtrate evaporated to a solid. The *phenylurea* (1·1 g.) separated from ethanol as needles, m. p. 188° (Found: C, 55·35; H, 4·85; N, 11·3. $C_{11}H_{11}O_2N_2Cl$ requires C, 55·35; H, 4·6; N, 11·75%).

6-*Methyl*-1-*phenyluracil*.—The preceding phenylurea (0·57 g.) was warmed with 2N-sodium hydroxide (4 ml.) for 10—15 min. at 100°. The clear solution was cooled and a precipitate of phenylurea (0·15 g.), m. p. and mixed m. p. 147°, filtered off. The filtrate with acid gave 6-*methyl*-1-*phenyluracil* (0·05 g.) which crystallised from water as plates, m. p. 276° (Found: C, 65·1; H, 5·15; N, 13·6. $C_{11}H_{10}O_2N_2$ requires C, 65·35; H, 5·0; N, 13·85%), $\lambda_{max.}$ 265 mμ (ε 12,800) in ethanol.

N-β-*Chlorocrotonoyl*-N′-*methylurea*.—A mixture of β-chlorocrotonyl chloride (2·4 g.), silver cyanate (7·1 g.), and benzene (20 ml.) was boiled under reflux for 1 hr., then decanted into 33% ethanolic methylamine (4 ml.) and filtered, and the filtrate was evaporated *in vacuo*. The residue solidified with ethanol. The *methylurea* (0·39 g.) separated from ethanol as prisms, m. p. 154° (Found: C, 40·95; H, 5·2; N, 15·4. $C_6H_9O_2N_2Cl$ requires C, 40·8; H, 5·1; N, 15·85%). It (0·2 g.) was warmed for 10 min. with 2N-sodium hydroxide (2 ml.). The solution was acidified and extracted with ethyl acetate, and the dried extract evaporated to give 1 : 6-dimethyluracil (0·03 g.), m. p. and mixed m. p. 210—220°.

N-*Acetoacetylurethane*.—Diketen (25 g.) was added to a cold solution of urethane (20 g.) in acetic acid (75 ml.). The solution was boiled under reflux for 25 min., then evaporated *in vacuo* to a crystalline residue. N-*Acetoacetylurethane* (11·7 g.) separated from benzene as needles, m. p. 77—78° (Found: C, 48·8; H, 6·4; N, 8·0. $C_7H_{11}O_4N$ requires C, 48·55; H, 6·4; N, 8·1%). A further quantity of the urethane (6·8 g.) was obtained by evaporation of the benzene solution. The compound gave a red colour with ferric chloride in ethanol.

Reaction of N-*Acetoacetylurethane with Primary Amines*.—(*a*) The urethane (0·2 g.) was

heated on a steam-bath with aqueous 20% methylamine (5 ml.) for 20 min. The cooled solution was acidified and extracted with ethyl acetate. Evaporation of the dried extract gave 1 : 6-dimethyluracil (0·1 g.), m. p. and mixed m. p. 220—222°. (*b*) The urethane (1·5 g.) in ethanol (5 ml.) was treated with ethylamine (1 ml.). The warm solution was evaporated *in vacuo* to a solid residue. N-β-*Ethylaminocrotonoylurethane* (1·4 g.) separated from light petroleum (b. p. 60—80°) as needles, m. p. 99° (Found: C, 50·8; H, 7·9; N, 12·95. $C_9H_{16}O_3N_2,\frac{1}{4}H_2O$ requires C, 50·6; H, 8·2; N, 13·0%). (*c*) The urethane (0·2 g.) and propylamine (0·2 ml.) similarly gave N-β-*propylaminocrotonoylurethane* (0·18 g.) as needles [from light petroleum (b. p. 60—80°)], m. p. 110° (Found: C, 56·2; H, 8·3; N, 13·0. $C_{10}H_{18}O_3N_2$ requires C, 56·05; H, 8·45; N, 13·1%). (*d*) The starting urethane (2 g.) and *cyclo*hexylamine (1·5 ml.) in ethanol (5 ml.) gave N-β-cyclo*hexylaminocrotonoylurethane* (2 g.) which crystallised from light petroleum (b. p. 80—100°) as needles, m. p. 119° (Found: C, 61·45; H, 8·55; N, 10·95. $C_{13}H_{22}O_3N_2$ requires C, 61·4; H, 8·7; N, 11·0%). (*e*) The urethane (0·2 g.) and aniline (0·2 ml.) gave N-β-*anilinocrotonoylurethane* (0·21 g.) which crystallised from ethanol as needles, m. p. 107° (Found: C, 62·9; H, 6·25; N, 11·2. $C_{13}H_{16}O_3N_2$ requires C, 62·9; H, 6·5; N, 11·3%).

Preparation of 6-*Methyluracils*.—(*a*) *N*-β-Ethylaminocrotonoylurethane (1·2 g.) in collidine (2 ml.) was boiled under reflux for 1 hr. The cooled solution gave a crystalline precipitate; 1-ethyl-6-methyluracil (0·25 g.) separated from ethyl acetate–light petroleum (b. p. 40—60°) as needles, m. p. 195° (Found: N, 18·2. Calc. for $C_7H_{10}O_2N_2$: N, 18·2%); Behrend and Buckendorff [8] give m. p. 195°. (*b*) *N*-β-Propylaminocrotonoylurethane (0·2 g.) similarly gave 6-*methyl*-1-*propyluracil* (0·18 g.) which separated from ethanol as needles, m. p. 173° (Found: N, 17·3. $C_8H_{12}O_2N_2$ requires N, 16·65%). (*c*) *N*-β-*cyclo*Hexylaminocrotonoylurethane (3·3 g.) was heated at 170° (bath) for 1 hr. The melt was cooled to give a semi-solid residue. This was extracted with dilute sodium hydroxide and filtered from an insoluble oil. The filtrate was just neutralised, to precipitate 1-cyclo*hexyl*-6-*methyluracil* (1·3 g.) which recrystallised from ethanol as needles, m. p. 233—235° (Found: C, 63·35; H, 7·7; N, 13·6. $C_{11}H_{16}O_2N_2$ requires C, 63·45; H, 7·75; N, 13·45%). (*d*) *N*-β-Anilinocrotonoylurethane (0·5 g.) was heated on a steam-bath with 2N-sodium hydroxide (2 ml.) and ethanol (2 ml.) for 1 hr. The solution was evaporated to about 1 ml. and carefully acidified to precipitate 6-methyl-1-phenyluracil (0·11 g.), m. p. and mixed m. p. with the material obtained from chlorocrotonic acid (see above), 275—276°. An improved yield of the uracil (75%) was obtained when the cyclisation was carried out in collidine as under (*a*).

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UNIVERSITY OF N.S.W., SYDNEY, AUSTRALIA. [*Received, November 10th*, 1958.]

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231. *Electrophilic Catalysis in Nucleophilic Substitution and Elimination. Part I. Kinetics and Mechanism of Reaction of* tert.*-Butyl Bromide with Alcohols, Phenols, and Carboxylic Acids in Nitromethane.*

By Y. Pocker.

Measurements are reported on the kinetics of reaction of *tert.*-butyl bromide with a variety of alcohols, phenols, and carboxylic acids in nitromethane. Superimposed on a common zero-order component with respect to hydroxylic reagent, the alcohols show a linear catalysis up to about 1·5M. From the linear slopes the catalytic order is found to be: $PhCH_2{\cdot}OH > MeOH > EtOH > Pr^nOH > Bu^nOH \sim Pr^iOH > Bu^sOH > Bu^tOH$.

With phenols, departures from linearity occur above *ca.* 0·3M and at lower concentrations the catalytic order is: $p\text{-}NO_2{\cdot}C_6H_4{\cdot}OH > p\text{-}CN{\cdot}C_6H_4{\cdot}OH > p\text{-}I{\cdot}C_6H_4{\cdot}OH > p\text{-}Br{\cdot}C_6H_4{\cdot}OH > p\text{-}Cl{\cdot}C_6H_4{\cdot}OH > PhOH > m\text{-}CH_3{\cdot}C_6H_4{\cdot}OH > p\text{-}CH_3{\cdot}C_6H_4{\cdot}OH > p\text{-}Bu^t{\cdot}C_6H_4{\cdot}OH > p\text{-}MeO{\cdot}C_6H_4{\cdot}OH$; *i.e.*, the acidity order. Phenols have a considerably higher electrophilic capacity to assist ionisation than alcohols.

In nitromethane, acetic and benzoic acids have a lower capacity to assist the ionisation of *tert.*-butyl bromide than phenols. It is suggested that this is because at 25·0° the carboxylic acids are largely in the form of cyclic dimers in this solvent.

The reactions of *tert.*-butyl bromide with water, ethyl alcohol, and phenol have been studied by Gelles, Hughes, and Ingold [1] in nitromethane. They showed that superimposed on the unimolecular process assisted only by solvent there is an electrophilic catalysis of ionisation which follows the acidity order PhOH > HOH > EtOH. We now extend their kinetic studies in an attempt to obtain a relative scale of electrophilic capacity of various hydroxylic reagents to assist the ionisation of alkyl halides in the non-hydroxylic, but polar solvent, nitromethane.

Experimental

Materials.—Nitromethane was dried, fractionated, and chromatographed as previously described.[2] Pyridine was purified by Burgess and Kraus's method,[3] dried (CaH_2), and fractionated, b. p. 115·2—115·6°, n_D^{25} 1·5067. *NN*-Dimethylaniline was dried (CaH_2) and fractionated, b. p. 193—194°. *N*-Methylaniline was similarly dried and fractionated, b. p. 195—196°. Aniline was dried (KOH), distilled from zinc under reduced pressure, and finally dried with calcium hydride and distilled from it, b. p. 184—184·5°, n^{25} 1·5832. Triethylamine was distilled from acetic anhydride to remove traces of primary and secondary amines, dried (CaH_2), and fractionated, b. p. 89—89·5°, n^{25} 1·3992. Tribenzylamine, recrystallised from ligroin and dried under vacuum (P_2O_5), had m. p. 92° *tert.*-Butyl bromide and methyl, ethyl, and benzyl alcohols were purified and dried as previously described: [4,5] Bu^tBr, b. p. 73—73·5°; MeOH, b. p. 64·2—64·6°, n^{25} 1·3266; d^{25} 0·7867; EtOH, b. p. 78—78·4°, n^{25} 1·3594, d^{25} 0·7850; $Ph{\cdot}CH_2{\cdot}OH$, b. p. 205—206°, n^{25} 1·5371, d^{25} 1·0413. *n*-Propyl alcohol was dried ($CaSO_4$, then Mg activated with I_2), and fractionated through a column of 20 theoretical plates. The middle fraction had b. p. 96·8—97·2°, n^{25} 1·3835. *iso*Propyl alcohol was freed from peroxides with solid stannous chloride, dried (CaO), and fractionated as above, b. p. 82—82·6°, n^{25} 1·3747. The butyl alcohols were dried (K_2CO_3) and fractionated after filtration of the desiccant. The redistilled alcohols were treated with the appropriate butyl phthalate and fractionated: Bu^nOH, b. p. 117·5—118°, n^{25} 1·3974; Bu^sOH, b. p. 99·5—100°, n^{25} 1·3961; Bu^tOH, b. p. 82·0—82·5°, m. p. 26°, supercooled to 25°, n^{25} 1·3823. The solid phenols were recrystallised

[1] Gelles, Hughes, and Ingold, *J.*, 1954, 2918.
[2] Pocker, *J.*, 1958, 240.
[3] Burgess and Kraus, *J. Amer. Chem. Soc.*, 1948, **70**, 706.
[4] de la Mare, Hughes, Ingold, and Pocker, *J.*, 1954, 2930.
[5] Hughes, Ingold, Mok, Patai, and Pocker, *ibid.*, 1957, 1220.

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from light petroleum and kept *in vacuo* over phosphoric oxide; PhOH, m. p. 43°; *p*-Cl·C_6H_4·OH, m. p. 43°; *p*-Br·C_6H_4·OH, m. p. 64°; *p*-I·C_6H_4·OH, m. p. 94°; *p*-CN·C_6H_4·OH, m. p. 113°; *p*-NO_2·C_6H_4·OH, m. p. 56°; *p*-Bu^t·C_6H_4·OH, m. p. 98·5°. The liquid phenols were chromatographed, dried ($CaSO_4$), and distilled: *m*-cresol, b. p. 190—191°; *p*-cresol, b. p. 201—202°, m. p. 34°; *p*-F·C_6H_4·OH, b. p. 82°/13 mm.

Kinetic Measurements.—Reaction mixtures, made up to 50 c.c. in glass-stoppered flasks, were prepared as previously described by weighing of separate standard solutions in nitromethane of the reactants. The thermostat was at 25·0° ± 0·02°. For the determination of " acid " (either as free HBr or as a salt of a weak amine with HBr), aliquot portions (5 c.c.) were run into dry acetone (50 c.c.) at −80° and titrated with standard sodium methoxide (lacmoid). In the presence of strong base (*e.g.*, triethylamine) the extent of reaction was determined by titrating (lacmoid) the free base, left after various periods of heating, with a standard methanolic solution of acid. For the determination of bromide ions a potentiometric titration with silver nitrate was carried out; two methods were used for the preparation of samples withdrawn from the kinetic runs. In the first (the " extraction " method) the sample was delivered into carbon tetrachloride (40 c.c.) at −10°, and this solution shaken three times with 20 c.c. of ice-cold water. In the second (the " evaporation " method) the sample was run into a flask immersed in a freezing mixture, evaporated with the help of a high capacity pump, and the residue was dissolved in water.

For the determination of olefin a sealed-ampoule technique was used; the sample, freed from amine, was added to methanolic bromine at −30°, solid potassium iodide was introduced, and the liberated iodine titrated with thiosulphate.

Results.—In the absence of added hydroxylic reagents, the rates of pyridinium ion (" acid ") production from *tert.*-butyl bromide and pyridine in nitromethane are of the first order in alkyl halide and zero order in pyridine.[1] This observation is now extended to cover a 1000-fold variation in pyridine and a 100-fold variation in *tert.*-butyl bromide (Table 1). The replacement

TABLE 1. *Initial first-order rate coefficients for " acid " production, k_1 (H^+) (sec.$^{-1}$), from* tert.*-butyl bromide and pyridine in nitromethane at* 25·0°.

[Bu^tBr]	0·020	0·020	0·020	0·020	0·002	0·020	0·200	
[C_5H_5N]	0·0002	0·002	0·020	0·20	0·020	0·020	0·020	
$10^5k_1(H^+)$	0·369	0·366	0·367	0·365	0·370	0·367	0·361	
[Bu^tBr] = [C_5H_5N]	0·01	0·02	0·04	0·08	0·20	0·50	1·00	2·00
$10^5k_1(H^+)$	0·366	0·367	0·364	0·367	0·367	0·369	0·370	0·370

of pyridine by other weak tertiary amines (*e.g.*, *NN*-dimethylaniline and tribenzylamine) of variable steric requirements leaves the rates of " acid " production substantially the same. Also, the rates of " acid," olefin, and bromide-ion production are practically identical (Table 2), indicating that with weak tertiary amines and in the absence of hydroxylic reagents an *E*1 process is under observation. With primary and secondary amines which are relatively weak bases (*e.g.*, aniline and *N*-methylaniline) and with strong tertiary amines (*e.g.*, triethylamine) the results are substantially the same except for a small increase in rate with increasing amine concentration, which has the characteristics of a bimolecular component of the S_N2 type. Thus, while the first-order rate coefficient of olefin production (Table 2) is the same as with pyridine and independent of amine concentration, the corresponding first-order rate coefficients of acid or bromide-ion production rise linearly with amine concentration. The linear rate coefficients for the reactions in presence of pyridine, *N*-methylaniline, aniline, and triethylamine respectively at 25·0° are $10^5k_2 = 0{\cdot}367 + 0{\cdot}00[C_5H_5N]$, $0{\cdot}367 + 0{\cdot}03$[Ph·NHMe], $0{\cdot}367 + 0{\cdot}20$[Ph·NH_2], $0{\cdot}367 + 1{\cdot}2[NEt_3]$. The second-order rate coefficients are: for methylaniline, $k_2 \sim 0{\cdot}3 \times 10^{-6}$, aniline $k_1 \sim 0{\cdot}2 \times 10^{-5}$, and for triethylamine $k_2 \sim 1{\cdot}2 \times 10^{-5}$ sec.$^{-1}$ l. mole^{-1}. In the first two amines the substitution products are Ph·NMeBu^t and Ph·NHBu^t respectively, but with triethylamine Bu^tOH was recovered. This is understandable if one realises that the *tert.*-butyl group cannot form substitution products with tertiary amines; the second-order component with strong tertiary amines may conceivably be due to a bimolecular attack by $CH_2{:}NO_2^-$ (formed in the reaction $CH_3{\cdot}NO_2 + Et_3N \rightleftharpoons CH_2{:}NO_2^- + Et_3\overset{+}{N}H$) on Bu^tBr to produce an unstable ester of *aci*-nitromethane which subsequently decomposes to *tert.*-butyl alcohol.

Reaction with alcohols, phenols, and carboxylic acids. The chemical processes in the reactions

of *tert.*-butyl bromide with hydroxylic reagents consist of simultaneous elimination and substitution. In the absence of substances which reduce the acidity of the hydrogen bromide in nitromethane these changes come to equilibrium only after a small amount of change because the reverse processes are even faster. But in the presence of a small excess of a weak tertiary amine they proceed to completion and the acid and bromide ion appear as amine hydrobromide.

TABLE 2. *First-order rate coefficients (sec.$^{-1}$) of acid, $k_1(H^+)$, bromide ion, $k_1(Br^-)$, and olefin, k_1(olefin), production from* tert.*-butyl bromide in the presence of amines in nitromethane at* 25·0°.

Bu^tBr = 0·05M.

Concn.	$10^5k_1(H^+)$	$10^5k_1(Br^-)$	10^5k_1(olefin)	Concn.	$10^5k_1(H^+)$	$10^5k_1(Br^-)$	10^5k_1(olefin)
	Pyridine				*N*-Methylaniline		
0·02	0·367	0·370	0·364	0·20	0·367	—	—
0·20	0·370	0·368	—	1·00	0·39	0·40	—
2·00	0·365	0·370	0·360	2·00	0·430	0·43	0·365
	NN-Dimethylaniline				Aniline		
0·02	0·367	0·369	0·365	0·20	0·41	—	0·367
0·20	0·364	0·365	—	0·50	0·47	0·46	—
2·00	0·372	0·374	0·350	1·00	0·56	0·57	0·360
	Tribenzylamine				Triethylamine		
0·20	0·367	0·365	—	0·0002	0·367	—	—
2·00	0·363	0·369	0·36	0·002	0·375	—	—
				0·01	0·40	0·49	0·37
				0·02	0·61	—	—

The relation between first-order rate coefficients of " acid " production and the concentration of various hydroxylic reagents is given in Table 3. These data show that the rates

TABLE 3. *Initial first-order rate coefficients, 10^5k_1 (sec.$^{-1}$), for acid production in the reaction of* tert.*-butyl bromide with various alcohols* (ROH), *phenols* (ArOH), *and carboxylic acids* ($R{\cdot}CO_2H$) *in the presence of pyridine in nitromethane at* 25·0°. $[Bu^tBr] = [C_5H_5N] =$ 0·050. When $[ROH] = 0{\cdot}00$, $k_1 = 0{\cdot}367 \times 10^5$ sec.$^{-1}$.

[ROH]	$Ph{\cdot}CH_2{\cdot}OH$	MeOH	EtOH	Pr^nOH	Pr^iOH	Bu^nOH	Bu^sOH	Bu^tOH
0·10	0·45	0·44	0·42	0·39	0·38	0·38	0·37	0·36
0·20	0·54	0·51	0·47	0·41	0·39	0·40	0·39	0·37
0·30	0·62	0·58	0·51	0·44	0·41	0·41	0·40	0·37
0·50	0·80	0·72	0·62	0·48	0·44	0·44	0·42	0·38
0·75	1·01	0·91	0·74	0·54	0·48	0·48	—	—
1·00	1·23	1·09	0·88	0·60	0·51	0·52	0·48	0·40
1·50	1·66	1·44	1·10	—	—	—	—	—
2·00	2·09	1·83	1·38	—	0·66	0·66	0·58	0·43
2·50	2·65	2·30	—	—	0·80	0·75	0·65	—
3·00	3·35	2·70	—	—	—	0·80	0·64	0·46
4·00	—	4·00	—	1·22	0·78	0·80	0·62	0·46

[$X{\cdot}C_6H_4{\cdot}OH$]	*p*-NO_2	*p*-CN	*p*-I	*p*-Br	*p*-Cl	*p*-F	H	*m*-Me	*p*-Me	*p*-Bu^t	*p*-MeO
0·10	0·93	0·87	0·69	0·68	0·65	0·64	0·62	0·61	0·61	—	0·59
0·15	1·21	1·12	—	—	0·80	0·79	0·70	—	—	0·72	—
0·20	1·5	1·36	1·04	1·00	0·98	0·92	0·87	0·86	0·85	0·84	0·82
0·25	1·75	1·62	—	—	—	—	—	—	—	0·95	0·94
0·30	2·1	1·87	1·34	—	1·30	1·21	1·17	1·13	1·08	1·07	1·05
0·40	3·00	2·4	1·66	1·63	1·60	1·49	1·42	1·39	1·33	1·31	—
0·50	4·2	—	—	—	2·20	—	1·99	1·65	1·61	—	1·50
0·80	7·2	—	—	—	—	—	3·00	—	—	—	—
1·00	—	—	—	—	—	—	—	3·7	3·2	—	—

[$Ph{\cdot}CO_2H$]...	0·04	0·16	0·32	[$Me{\cdot}CO_2H$]	0·26	0·65	0·87	1·95	3·25
10^5k_1	0·41	0·51	0·69	10^5k_1	0·56	0·85	1·18	1·54	2·65

increase linearly with alcohol concentration up to about 1·5M, whereupon departures from linearity occur. These departures are accelerative with methyl, ethyl, and benzyl alcohols and decelerative for *iso*propyl and *n*-, *sec.*-, and *tert.*-butyl alcohols.

With phenols the rate increase is almost linear up to between 0·3 and 0·5M (the actual value depending on the phenol), whereat a " more than linear catalysis " sets in.

Only two carboxylic acids have been examined, acetic and benzoic. Both show a lower catalytic capacity than phenols. Acetic acid was examined up to 3·25M, and the departure from linearity was apparent above *ca.* 0·80M, whereat a deceleration occurs.

The linear rate coefficients, 10^5k_1 (sec.$^{-1}$), for reactions in presence of alcohols respectively are 0·367 + 0·86[$PhCH_2OH$], 0·367 + 0·72[MeOH], 0·367 + 0·49[EtOH], 0·367 + 0·23[Pr^nOH], 0·367 + 0·15[Pr^iOH], 0·367 + 0·15[Bu^nOH], 0·367 + 0·11[Bu^sOH], 0·367 + 0·03[Bu^tOH].

With phenols, the *initial* slopes are of the form: $10^5k_1 = 0·367 + k_2$[ArOH] from which the following catalytic coefficients, 10^5k_2 (sec.$^{-1}$ l. mole^{-1}) are obtained: *p*-NO_2·C_6H_4·OH 5·6, *p*-Br·C_6H_4·OH 3·16, PhOH 2·68, *p*-Bu^t·C_6H_4·OH 2·35, *p*-CN·C_6H_4·OH 5·0, *p*-Cl·C_6H_4·OH 3·10, *m*-Me·C_6H_4·OH 2·55, *p*-MeO·C_6H_4·OH 2·28 *p*-I·C_6H_4·OH 3·25, *p*-F·C_6H_4·OH 2·8, *p*-CH_2·C_6H_4·OH 2·4.

Discussion

In the region of linear catalysis the order of decreasing efficiency in alcohols (EtOH = 1) is: $Ph·CH_2·OH$ (1·75) > MeOH (1·47) > EtOH (1·00) > Pr^nOH (0·47) > Bu^nOH (0·30) ~ Pr Pr^iOH (0·30) > Bu^sOH (0·225) > Bu^tOH (~0·06). With the exception of benzyl alcohol this is the accepted order of decreasing acidity. It is unlikely that the special position of benzyl alcohol is due to a nucleophilic component. It may be that when we refer to alcohols in nitromethane, we refer to the fraction which is free to form hydrogen bonds (monomers) and that this fraction is particularly high in benzyl alcohol. According to its acidity, benzyl alcohol is placed after ethanol.

The "more than linear" catalysis is shown by hydroxylic reagents which, when solvents, are more ionising media towards *tert.*-butyl bromide than nitromethane. Indeed, the alcohols which at high concentration show a "less than linear" catalysis are, when solvents, poorer ionising media than nitromethane. This means that in addition to the hydrogen-bonding molecule which is responsible for the linear catalysis, one or more hydroxylic molecules intrude among the nitromethane molecules in the solvation shell of the transition state leading to a more than or less than linear increase in the ionisation rate, as the case may be.

The phenols follow at low concentration the acidity order. Indeed a linear correlation exists between the logarithm of the initial catalytic slope of a given phenol and its pK_a in water. Since the ionisation of phenols in water conforms with the Hammett equation $\log (K_{ArOH}/K_{PhOH}) = \rho\sigma$, one would also expect the logarithm of the ratio of the catalytic coefficients $\log (k_{2(ArOH)}/k_{2(PhOH)})$ to be directly proportional to the σ constants of the phenols.[6] This is confirmed by Table 4 where $\rho = 0·27 \pm 0·03$.

TABLE 4.

Subst.	σ	$\log (k_{2(ArOH)}/k_{2(PhOH)})$	ρ	Subst.	σ	$\log (k_{2(ArOH)}/k_{2(PhOH)})$	ρ
p-MeO	−0·268	−0·070	0·26	*p*-Cl	+0·0226	+0·064	0·28
p-Bu^t	−0·197	−0·057	0·29	*p*-Br	+0·232	+0·071	0·30
p-Me	−0·170	−0·048	0·28	*p*-I	+0·276	+0·83	0·30
m-Me	+0·069	+0·020	0·29	*p*-CN	+1·00	+0·270	0·27
p-F	+0·062	+0·018	0·29	*p*-NO_2	+1·27	+0·32	0·25

Acetic and benzoic acids show a capacity to assist the ionisation of *tert.*-butyl bromide in nitromethane which is only slightly higher than that of alcohols. A comparison with phenols on the basis of acid strength is misleading since if these carboxylic acids exist largely as cyclic dimers then they are not present under the kinetic conditions as the same species whose acid strength we determine in hydroxylic solvents.

Bartlett and Dauben [7] showed that the hydroxylic compounds which catalyse the rearrangement of camphene hydrochloride into *iso*bornyl chloride are all capable of increasing the acidity of hydrogen chloride in dioxan. Since hydrogen chloride in dioxan

[6] Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, 1940, p. 188; Hine, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, 1956, p. 72.

[7] Bartlett and Dauben, *J. Amer. Chem. Soc.*, 1940, **62**, 1339.

is present as the weaker acid, dioxanonium chloride from which the hydroxylic reagents employed by them were incapable of taking a proton, they were able to obtain a measure of the hydrogen-bonding capacity of these reagents with a chlorine atom. Indeed, the order they obtain agrees well with the present kinetic observations, *i.e.*, *p*-$CN{\cdot}C_6H_4{\cdot}OH$ > *p*-$Cl{\cdot}C_6H_4{\cdot}OH$ > PhOH > *p*-$Me{\cdot}C_6H_4{\cdot}OH$ > $Me{\cdot}CO_2H$ > MeOH > EtOH > Pr^iOH. Thus in their case, too, acetic acid showed a catalytic capacity similar to that of alcohols.

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WILLIAM RAMSAY AND RALPH FORSTER LABORATORIES,
UNIVERSITY COLLEGE, GOWER ST., LONDON, W.C.1. [*Received, December 3rd*, 1958.]

232. *Molecular Polarisability. The Anisotropy of the* C=C *Bond.*

By R. BRAMLEY, C. G. LE FÈVRE, R. J. W. LE FÈVRE, and B. PURNACHANDRA RAO.

Molar Kerr constants and dielectric polarisations in carbon tetrachloride at 25° are recorded for *cis*- and *trans*-dichloro-, 1 : 1-dichloro-, trichloro-, and tetrachloro-ethylenes. Molecular anisotropies are also given for the three (of these five) chloroethylenes which are polar. The longitudinal and transverse polarisabilities of the C–Cl bond are obtained from carbon tetrachloride and chloroform and used to analyse the polarisability ellipsoid of 1 : 1-dichloroethylene. Longitudinal, tranverse, and vertical polarisabilities of the C=C link are deduced therefrom as $0{\cdot}28_0$, $0{\cdot}07_3$, and $0{\cdot}07_7 \times 10^{-23}$ c.c., respectively. These values are tested by application to ethylene and its other chloro-derivatives. Agreement between observed and calculated quantities is satisfactory. Available facts show that *cis*-dichloroethylene is non-planar.

To ascertain the anisotropy of polarisability of the C=C bond, we studied molar Kerr constants and other properties of five chlorinated ethylenes, and analysed them with the help of the known structures of these molecules. Among them, the fundamentally important case is vinylidene dichloride, $CH_2{=}CCl_2$, because in it the resultant dipole moment undoubtedly lies along the C=C bond, and thus along one of the principal axes of the molecular ellipsoid. Accordingly the required longitudinal, transverse, and vertical polarisabilities, $b_L^{C=C}$, $b_T^{C=C}$, and $b_V^{C=C}$ respectively, can be calculated; the values so obtained are of general applicability to ethylene and the other substances examined.

EXPERIMENTAL

Materials.—Carbon tetrachloride, used as solvent throughout, was dried ($CaCl_2$), slowly fractionated (1 m. column packed with glass helices), and stored over calcium chloride. The isomeric dichloroethylenes were obtained from a B.D.H. " technical " grade. This, after being dried (K_2CO_3), was fractionally distilled under oxygen-free nitrogen in absence of light. The following fractions were collected: *trans*-dichloroethylene, b. p. 47·40° ± 0·005°/757·6 ± 0·05 mm., $n_D^{25} = 1{\cdot}44348$; *cis*-dichloroethylene, b. p. 59·85—59·90°/759·2—760·0 mm., $n_D^{25} = 1{\cdot}44615$. These were sealed and kept in the dark. Trichloro- and tetrachloro-ethylenes were specially prepared and fractionated samples (presented by Imperial Chemical Industries, Australia and New Zealand, Limited, whom we thank) with b. p. and n_D^{25} respectively of 86·4—86·6°/760 mm., 1·47503, and 120—122°/760 mm., 1·50328; they also were preserved out of the light. Vinylidene dichloride was obtained by treatment of 1 : 1 : 2-trichloroethane (also presented as above) with lime (cf. Beilstein s " Handbuch," 3rd suppl., Vol. 1, p. 647), b. p. 31·4—32·0°/760 mm.

Apparatus, Techniques, and Methods of Calculation.—These were as described previously.[1-6]

[1] Le Fèvre and Le Fèvre, *J.*, 1953, 4041; 1954, 1577.
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[5] Buckingham, Chau, Freeman, Le Fèvre, N. Rao, and Tardif, *J.*, 1956, 1405.
[6] Le Fèvre and P. Rao, *J.*, 1957, 3644; 1958, 1465.

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TABLE 1. *Depolarisation factors for solutions in carbon tetrachloride.**

Solute: *cis*-Dichloroethylene					
$10^5 f_2$	3753	7379	11106	14256	16969
$10^5 \Delta_{12}$	5·873	8·370	10·52	13·00	14·90
Solute: 1 : 1-Dichloroethylene					
$10^5 f_2$	1559·5	2509	3349·5	3966	5044
$10^5 \Delta_{12}$	5·391	6·062	6·589	6·968	7·635
Solute: Trichloroethylene					
$10^5 f_2$	1592	4278	6591	9378·5	11762·5
$10^5 \Delta_{12}$	5·246	8·175	10·54	13·12	16·39

* $\Delta_1 = 0{\cdot}0346$ for $f_2 = 0$.

TABLE 2. *Dielectric constants, densities, refractive indexes, and Kerr constants as functions of weight fractions for solutions in carbon tetrachloride * at 25°.*

cis-Dichloroethylene

$10^5 w_2$	1225	1866	2596	3082	3666	4073
ε_{12}	2·3059	2·3463	2·3936	2·4249	2·4626	2·4890
d_{12}	1·57965	1·57719	1·57432	1·57239	1·57038	1·56853
$10^4 \Delta n$	0	−2	−3	−4	−5	−7
$10^5 w_2$	5810	6903	7181	9213	14121	16445
$10^7 \Delta B$	0·037	0·041	0·043	0·057	0·087	0·108

whence $\Sigma\Delta\varepsilon/\Sigma w_2 = 6{\cdot}423$; $\Sigma\Delta d/\Sigma w_2 = -0{\cdot}3924$; $\Sigma\Delta n/\Sigma w_2 = -0{\cdot}0127$; $\Sigma w_2\Delta B/\Sigma w_2^2 = 0{\cdot}630_6$.

trans-Dichloroethylene.

$10^5 w_2$	546	1576	1603	1824	3010	3655	4411	4735·5	8069
ε_{12}	2·2268	2·2262	2·2257	2·2257	2·2247	2·2246	2·2239	2·2239	—
d_{12}	1·58201	1·57756	1·57742	1·57652	1·57125	1·56857	1·56544	1·56497	—
$10^4 \Delta n$	−4	−10	−10	−10	−11	−12	−12	−15	−20
$10^5 w_2$	1107	1694·5	3350	3366	4187	8069			
$10^7 \Delta B$	0·011	0·014	0·029	0·029	0·034	0·071			

whence $\Sigma\Delta\varepsilon/\Sigma w_2 = -0{\cdot}0678$; $\Delta d = -0{\cdot}4643 w_2 + 0{\cdot}895 w_2^2$; $\Sigma\Delta n/\Sigma w_2 = 0{\cdot}0353$; $\Sigma w_2\Delta B/\Sigma w_2^2 = 0{\cdot}865_8$.

1 : 1-Dichloroethylene

$10^5 w_2$	349	441	567	625	1030	1125·5
ε_{12}	2·2378	2·2401	2·2440	2·2471	2·2572	2·2616
d_{12}	1·58279	1·58228	1·58169	1·58149	1·57941	1·57902
$10^4 \Delta n$	—	—	—	−2	—	−3
$10^5 w_2$	1341	2211	2533	3227·5	4057	4724
ε_{12}	2·2671	2·2928	2·3019	2·3226	2·3469	2·3665
d_{12}	1·57809	1·57393	1·57240	1·56909	1·56523	1·56207
$10^4 \Delta n$	−3	−6	−7	−10	−13	−14
$10^5 w_2$	198	413	984	1347	1545	2709
$10^7 \Delta B$	0·008	0·015	0·033	0·043	0·054	0·089

whence $\Sigma\Delta\varepsilon/\Sigma w_2 = 2{\cdot}976$; $\Sigma\Delta d/\Sigma w_2 = -0{\cdot}4767$; $\Sigma\Delta n/\Sigma w_2 = -0{\cdot}0292$; $\Sigma w_2\Delta B/\Sigma w_2^2 = 3{\cdot}32_4$.

Trichloroethylene

$10^5 w_2$	932	1251	1644	1650	2142	2184	2385	2647·5	
ε_{12}	2·2370	2·2408	2·2451	2·2449	2·2502	2·2512	2·2533	2·2583	
d_{12}	1·58320	1·58270	1·58218	1·58220	1·58142	1·58141	1·58114	1·58054	
$10^5 w_2$	202	604	1209	1726	3369	4317	$10^5 w_2$	12117	12692	12878
$10^7 \Delta B$	0·004	0·006	0·012	0·018	0·033	0·045	$10^4 \Delta n$	21	21	23

whence $\Sigma\Delta\varepsilon/\Sigma w_2 = 1{\cdot}111$; $\Sigma\Delta d/\Sigma w_2 = -0{\cdot}1451$; $\Sigma\Delta n/\Sigma w_2 = 0{\cdot}0172$; $\Sigma w_2\Delta B/\Sigma w_2^2 = 0{\cdot}97_8$.

Tetrachloroethylene

$10^5 w_2$	802	1619	2189	3167	3900	4543	5351	5652
ε_{12}	2·2274	2·2278	—	2·2286	2·2290	2·2302	2·2297	2·2301
d_{12}	1·58477	1·58505	1·58523	1·58542	1·58558	1·58578	1·58596	1·58606
$10^4 \Delta n$	0	5	6	11	14	16	20	21
$10^5 w_2$	2876	3958	6462	7118	10248	11748		
$10^7 \Delta B$	0·020	0·028	0·043	0·050	0·070	0·079		

whence $\Sigma\Delta\varepsilon/\Sigma w_2 = 0{\cdot}0551$; $\Delta\Sigma d/\Sigma w_2 = 0{\cdot}0277$; $\Sigma\Delta n/\Sigma w_2 = 0{\cdot}0342$; $\Sigma w_2\Delta B/\Sigma w_2^2 = 0{\cdot}681$.

* Values for $w_2 = 0$, $\varepsilon_1 = 2{\cdot}2270$, $d_1 = 1{\cdot}58454$, $n_1 = 1{\cdot}4574$ (Na-D light), $B_1 = 0{\cdot}070 \times 10^{-7}$ (Na-D light).

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Observations are listed in Tables 1—4, wherein symbols have the following meanings: w_2, weight fraction; f, molar fraction; Δ, depolarisation factor; ε, dielectric constant; d, density; n, refractive index; B, Kerr constant; suffixes 1, 2, and 12 denote respectively solvent, solute, and solution; $\Delta\Delta$, $\Delta\varepsilon$, Δd, etc., represent alterations of the property concerned from solvent to solution; ${}_{\infty}\delta_2{}^2$ is the molecular anisotropy at infinite dilution, and is different from δ in Table 4; α, β, γ, and δ are coefficients in the equations $\varepsilon_{12} = \varepsilon_1(1 + \alpha w_2)$, $d_{12} = d_1(1 + \beta w_2)$, $n_{12} = n_1(1 + \gamma n_1)$, and $B_{12} = B_1(1 + \delta w_2)$; ${}_{\infty}({}_{\mathrm{m}}K_2)$ and ${}_{\infty}P_2$ are molar Kerr constants and total dielectric polarisations at infinite dilution; R_{D}, ${}_{\mathrm{E}}P$, ${}_{\mathrm{D}}P$, and μ indicate molar refractions

TABLE 3. *Molecular anisotropies of solutes at infinite dilution.*

Solute	R.H.S. of equation giving $\Delta\Delta_{12}$	D *	$10^3\,{}_{\infty}\delta_2{}^2$
cis-$C_2H_2Cl_2$	$0{\cdot}6261f_2 + 0{\cdot}272f_2{}^2$	−0·2225	$31{\cdot}5_2$
1 : 1-$C_2H_2Cl_2$	$0{\cdot}7165f_2 - 1{\cdot}18f_2{}^2$	−0·3085	$35{\cdot}7_1$
C_2HCl_3	$1{\cdot}048f_2 + 0{\cdot}275f_2{}^2$	−0·1200	$51{\cdot}2_1$

* D is given by $d_{12} = d_1 + Df_2$.

TABLE 4. *Calculation of results.*

Solute	$(\alpha\varepsilon_1)_{w_2=0}$	$(\beta)_{w_2=0}$	γ	$(\delta)_{w_2=0}$	$10^{12}\,{}_{\infty}({}_{\mathrm{m}}K_2)$	${}_{\infty}P_2$ (c.c.)	R_{D} (c.c.)
cis-$C_2H_2Cl_2$ ...	$6{\cdot}42_2$	$-0{\cdot}247_6$	−0·009	$9{\cdot}0_1$	$5{\cdot}2_5$	$88{\cdot}1_3$	$20{\cdot}25$ [a]
trans-$C_2H_2Cl_2$	−0·06[8]	$-0{\cdot}293_0$	−0·024	$12{\cdot}3_6$	$9{\cdot}9_6$	$22{\cdot}2_8$	$20{\cdot}60$ [a]
1 : 1-$C_2H_2Cl_2$ ...	$2{\cdot}97_6$	$-0{\cdot}300_8$	−0·020	$47{\cdot}4_9$	$34{\cdot}4_2$	$53{\cdot}6_7$	$20{\cdot}43$ [a]
C_2HCl_3	$1{\cdot}11_1$	$-0{\cdot}091_6$	0·012	$13{\cdot}9_7$	$14{\cdot}2_9$	$41{\cdot}7_4$	$25{\cdot}42$ [f]
C_2Cl_4	$0{\cdot}05_5$	$0{\cdot}017_5$	$0{\cdot}023_5$	$9{\cdot}7_2$	$13{\cdot}2_4$	$30{\cdot}8_3$	$30{\cdot}33$ [h]

Solute	${}_{\mathrm{E}}P$ (c.c.)	${}_{\mathrm{D}}P$ (c.c.)	μ (D)	$10^{35}(\theta_1 + \theta_2)$	$10^{23}(b_1 + b_2 + b_3)$	$10^{46}\Sigma(b_1 - b_1)^2$	$10^{35}\theta_2$
cis-$C_2H_2Cl_2$ ...	19·62 [b]	21·6 [c]	1·80	$1{\cdot}24_8$	$2{\cdot}33_3$	17·16	0·228
trans-$C_2H_2Cl_2$	19·92 [b]	22·3 [d]	0	$2{\cdot}36_6$	$2{\cdot}36_9$	—	—
1 : 1-$C_2H_2Cl_2$ ...	19·78 [f]	21·8 [b]	1·25	$8{\cdot}18_5$	$2{\cdot}35_2$	19·75	7·011
C_2HCl_3	24·61 [f]	27·1 [e]	0·85	$3{\cdot}39_8$	$2{\cdot}92_6$	43·84	0·793
C_2Cl_4	29·81 [h]	30·8 [d]	0	$3{\cdot}14_9$	$3{\cdot}54_5$	—	—

[a] Calc. from Timmermans, "Physico-chemical Constants of Pure Organic Compounds," Elsevier, New York and London, 1950, pp. 277/8. [b] Extrapolated from R_α and R_β calc. from a. [c] Taken as ${}_{\mathrm{E}}P \times 1{\cdot}1$. [d] *I.e.*, ${}_{\infty}P_2$. [e] From Schildknecht, "Vinyl and Related Polymers," Wiley, New York, 1952, p. 449. [f] *I.e.*, $0{\cdot}968R_{\mathrm{D}}$; cf. ratios ${}_{\mathrm{E}}P/R_{\mathrm{D}}$ for *cis*- and *trans*-isomers. [g] From Beilstein, 3rd Suppl., Vol. 1. [h] Calc. from refractions listed in Landolt and Börnstein's Tables, 1912 Edn.

TABLE 5. *Semi-axes of polarisability ellipsoids.*

	$10^{23}b_1$	$10^{23}b_2$	$10^{23}b_3$
$CH_2{:}CCl_2$	0·896	0·879	0·575
cis-$C_2H_2Cl_2$	$0{\cdot}779_5$	0·946	0·608
C_2HCl_3	1·003	1·231	0·692

(sodium light), electronic and distortion polarisations, and dipole moments; b_1, b_2, and b_3 are semi-axes of a molecular polarisability ellipsoid; θ_1 and θ_2 are explained and expanded in ref. 2.

Molecular Semi-axes from Experiment.—Semi-axes of the polarisability ellipsoids for the three polar solutes are given in Table 5. They have been calculated on the assumption that $\mu_{\mathrm{resultant}}$ in each case is acting parallel to one of the semi-axes; this may not be valid for trichloroethylene although it obviously is so for the other two molecules. Semi-axes for the non-polar compounds cannot, of course, be obtained directly from experiment (see ref. 2, p. 287).

Previous Measurements.—Dielectric polarisation measurements in carbon tetrachloride have been previously recorded only for trichloroethylene, to which a polarity of 0·8 D is ascribed.[7] Other determinations, either in benzene or "unspecified solvents," are: 1 : 1-dichloroethylene,[8] 1·30 or 1·18 D, *cis*-dichloroethylene,[7] 1·74—1·89 D, *trans*-dichloroethylene,[7] 0—0·7 D, trichloroethylene,[7] 0·94 D, and tetrachloroethylene,[7] 0 D. As a vapour the *cis*-dichloro-compound shows [9] $\mu = 1{\cdot}90 \pm 0{\cdot}02$ D.

Sachsse [10] has stated, without giving observational details, that *cis*- and *trans*-dichloro- and

[7] Wesson, "Tables of Electric Dipole Moments," Technology Press, Massachusetts Inst. Technology, 1948.

[8] Rogers, *J. Amer. Chem. Soc.*, 1947, **69**, 1243; Errera, *Physikal. Z.*, 1926, **27**, 764.

[9] Maryott and Buckley, "Table of Dielectric Constants and Electric Dipole Moments of Substances in the Gaseous State," *Nat. Bur. Stand. Circular* 537, Washington, U.S.A., 1953.

[10] Sachsse, *Physikal. Z.*, 1935, **36**, 357.

tetrachloro-ethylenes in carbon tetrachloride at about 4° had ${}_mK$'s of 8·2, 8·4, and 12·8 × 10^{-12} respectively. The electric double refractions noted for the *cis*- and *trans*-dihalogeno-substances as gases by Stuart and Volkmann [11] correspond (according to Sachsse) to ${}_mK$'s of 7·5 and 18·6 × 10^{-12}.

No reference can be found to the depolarisation of light scattered by these five solutes either undiluted or dissolved.

Discussion

Derivation of Bond Polarisability Ellipsoid for C=C.—The desired values of $b_L^{C=C}$, $b_T^{C=C}$, and $b_V^{C=C}$ can be extracted from the molecular ellipsoid found (Table 5) for 1 : 1-dichloro-ethylene, provided that specifications are known for the structure of CH_2=CCl_2 and for the polarisability ellipsoids of the C–H and C–Cl bonds.

The C–H link, for reasons given before,[2,12] is taken as isotropic, *i.e.*, $b_L^{C-H} = b_T^{C-H} = b_V^{C-H} = 0{\cdot}064 \times 10^{-23}$ c.c. Information on C–Cl can be obtained from the molecules CCl_4 and $CHCl_3$. For the former,[13] $b_1 = b_2 = b_3 = 1{\cdot}026 \times 10^{-23}$ and for the latter $b_1 = 0{\cdot}673 \times 10^{-23}$ c.c. According to Allen and Sutton's list,[14] the Cl–C–Cl angles in CCl_4 and $CHCl_3$ are tetrahedral and 112° respectively, whence $b_L^{C-Cl} = 0{\cdot}399 \times 10^{-23}$ and $b_T^{C-Cl} = 0{\cdot}185 \times 10^{-23}$ c.c. From ref. 14 the configuration of CH_2=CCl_2 is set by a Cl–C–C angle of 122° ± 1°. The above facts, together with the appropriate trigonometrical quantities, lead to the equations for CH_2:CCl_2: $10^{23}b_1 = 0{\cdot}618 + b_L^{C=C}$; $10^{23}b_2 = 0{\cdot}806 + b_T^{C=C}$; and $10^{23}b_3 = 0{\cdot}498 + b_V^{C=C}$, from which, in turn, the bond semi-axes emerge as: $10^{23}b_L^{C=C} = 0{\cdot}280$ c.c.; $10^{23}b_T^{C=C} = 0{\cdot}073$ c.c.; and $10^{23}b_V^{C=C} = 0{\cdot}077$ c.c.

This is actually the second estimate of the anisotropy of polarisability of the C=C bond to be made completely from experiment, Sachsse [10] having reported 0·392, 0·094, and 0·035 × 10^{-23} for the three $b^{C=C}$'s in question. Since Sachsse depended upon the then available intervalency angles for calculation from his ${}_mK$'s (see above), we consider the present to be the more reliable. Wang [15] and Denbigh [16] quote values of 0·302 and 0·286 × 10^{-23} for $b_L^{C=C}$ but appear to have used the Kerr constant given in the literature for ethylene and assumed, without *a priori* justification, that $b_T^{C=C} = b_V^{C=C}$. Bolton [17] and Mueller,[18] by different theoretical routes, have deduced that $b_L^{C=C} = 0{\cdot}286$ or 0·312 × 10^{-23} c.c., respectively. An empirical connection with bond lengths [19] forecasts $b_L^{C=C} = 0{\cdot}275 \times 10^{-23}$.

Derivation of Molecular Ellipsoids of Non-polar Chloroethylenes.—Allen and Sutton [14] give intercentre distances and angles as follows: *trans*-$C_2H_2Cl_2$, C–Cl 1·69 ± 0·03 Å, Cl–Cl 4·7 Å, C–C–Cl angle 122·5° ± 1°; C_2Cl_4, C–C 1·38 or 1·34, both ±0·05 Å, C–Cl 1·71 or 1·73, both ±0·02 Å, C–C–Cl angle 122·2° or 123·7°, both ±1°. Taking for the former molecule a double bond length as in C_2Cl_4, we predict the semi-axes: $10^{23}b_1 = 1{\cdot}082$, $10^{23}b_2 = 0{\cdot}693$, and $10^{23}b_3 = 0{\cdot}575$ (b_1 lying through the Cl ... Cl centres); ${}_mK$ (calc.) is therefore 10·7 × 10^{-12} against 10·0 × 10^{-12} found. Improved agreement can be secured by appropriate variations of lengths and angles within the limits stated in ref. 14. If C–Cl is kept at 1·69 Å, but the angle C–C–Cl is put equal to 120°, ${}_mK$ calc. becomes 9·8 × 10^{-12}.

For tetrachloroethylene it is assumed that the double bond lies along the principal axis b_1. With the Cl–C–C angle at 122·0°, the polarisability semi-axes are $10^{23}b_1 = 1{\cdot}262$, $10^{23}b = 1{\cdot}426$, and $10^{23}b_3 = 0{\cdot}817$, or with the angle at 123·7° they are $10^{23}b_1 = 1{\cdot}284$, $10^{23}b_2 = 1{\cdot}405$, and $10^{23}b_3 = 0{\cdot}817$. The ${}_mK$'s computed for the two sets are 14·0 × 10^{-12} or 13·6 × 10^{-12} respectively, the " found " value being 13·2 × 10^{-12}.

[11] Stuart and Volkmann, *Ann. Phys.*, 1933, **18**, 121.
[12] Le Fèvre and Le Fèvre, *Chem. and Ind.*, 1955, 1121
[13] Armstrong, Aroney, Le Fèvre, and Smith, *J.*, 1958, 1474.
[14] Allen and Sutton, *Acta Cryst.*, 1950, **3**, 46.
[15] Wang, *J. Chem. Phys.*, 1939, **7**, 1012.
[16] Denbigh, *Trans. Faraday Soc.*, 1940, **36**, 936.
[17] Bolton, *Trans. Faraday Soc.*, 1954, **50**, 1261.
[18] Mueller, *J. Chem. Phys.*, 1954, **22**, 120.
[19] Le Fèvre, *Proc. Chem. Soc.*, 1958, 283.

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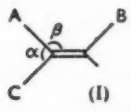
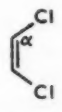
Prediction of Molar Kerr Constant of Ethylene.—The calculated semi-axes for this molecule are 0·536, 0·329, and 0·333 × 10^{-23}, whence $(b_1 - b_2)^2 + (b_2 - b_3)^2 + (b_3 - b_1)^2 = 0{\cdot}084 \times 10^{-46}$; ${}_mK$ is therefore $1{\cdot}9_1 \times 10^{-12}$, or, if the distortion and electronic polarisations recorded by Watson and Ramaswamy [20] are introduced, $1{\cdot}9_8 \times 10^{-12}$. Two determinations of B_{ethylene} are available: $0{\cdot}19_6 \times 10^{-10}$ at 20°/1 atm., and $\lambda = 5460$ Å, by Kuss,[21] or $0{\cdot}16_3 \times 10^{-10}$ at 0°, 1 atm., and $\lambda = 6500$ Å, by Breazeale; [22] these correspond to ${}_mK$'s of $1{\cdot}9_1$ or $1{\cdot}8 \times 10^{-12}$. Considering that the quoted B's are both extrapolated from observations taken at pressures considerably above normal, we cannot expect better agreement between ${}_mK_{\text{obs.}}$ and ${}_mK_{\text{calc.}}$.

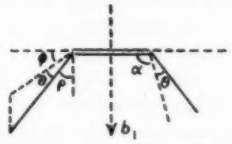
Applicability of Bond Polarisabilities to Trichloroethylene.—Interpretation of data for this case is difficult because the direction of action of the resultant dipole moment is not known exactly. α is 114° and β is 123° in (I).[14] It is highly probable that the axis of



(I)



(II)



(III)

maximum polarisability lies parallel to the bonds holding Cl atoms B and C. On such a basis the semi-axes calculable *a priori* would be: $10^{23}b_1 = 1{\cdot}01_6$, $10^{23}b_2 = 1{\cdot}21_7$, $10^{23}b_3 = 0{\cdot}69_6$. In deducing b_1, b_2, and b_3 from experiment (Table 5), the assumption was made that $\mu_{\text{resultant}}$ acts along one of the principal polarisability axes. Because of the smallness of $\mu_{\text{resultant}}$, *viz.*, 0·85D, the predicted and found b's should be compared to two significant figures only; when this is done, both sets become 1·0, 1·2, and 0·7 × 10^{-23}. Other dispositions of b_{maximum} were tried, but each resulted in a larger value for $b_{1\text{ calc.}}$. The implication therefore is that $\mu_{\text{resultant}}$ is acting along a line situated some 24° anticlockwise from the bond holding atom A; this seems reasonable.

Conformation of cis-1 : 2-*Dichloroethylene.*—The structure is specified in ref. 14 as (II). If the molecule is planar, the Cl–Cl distance (3·7 Å) and the C–Cl distance (1·67 Å) quoted (from *X*-ray diffraction on the gas) are not reconcilable with a Cl–C=C angle (α) of 123·5°, it necessitates either (*a*) an abnormally [14,23] long C=C bond (*ca.* 1·8 Å), or (*b*) a Cl–C=C angle of 135°. The semi-axes predicted for these two angles are: $b_1 = 0{\cdot}869$, $b_2 = 0{\cdot}908$, $b_3 = 0{\cdot}575 \times 10^{-23}$ (for ∠ Cl–C=C = 123·5°), $b_1 = 0{\cdot}785$, $b_2 = 0{\cdot}992$, $b_3 = 0{\cdot}575 \times 10^{-23}$ (for ∠ Cl–C=C = 135°) against values from experiment of $0{\cdot}779_5$, 0·946, and 0·608 × 10^{-23}, with which neither set is in good agreement. No variation about 3·7 Å is cited for the Cl–Cl separation but the likelihood of considerable error is diminished by the fact that the corresponding length (given as 4·7 Å) in the *trans*-isomer is close to that calculated (4·6 Å) from the appropriate molecular dimensions.

Accordingly non-planar models have been considered (III). Taking the C=C distance as 1·34 Å and that for C–Cl as 1·67 Å, we can evaluate an angle θ by geometry as 34° 23′; α is 123·5°; θ is the angle of projection of each C–Cl bond on the plane which contains the long axis of the double bond and is symmetrically between the two planes in which the two Cl–C=C triangles are lying; b_1 also must be situated in this plane, and the C–Cl moments will act at an angle ρ to b_1 (where ρ = 52° 13′). These data being used, b_1 (calc.) becomes 0·732 × 10^{-23}, while b_1 (expt.) = $0{\cdot}779_5 \times 10^{-23}$. Bearing in mind the fact that b_1 (calc.) is based on two different bond lengths, one atom–atom distance, and one electron-diffraction angle determination, we can accept the agreement reached.

Alternatively, more precise information on the angles θ, φ, and ρ can be obtainable from the measured quantity b_1, because there can be no doubt where b_1 lies with reference to the

[20] Watson and Ramaswamy, *Proc. Roy. Soc.*, 1936, *A*, **156**, 144.
[21] Kuss, "Elektro-optischer Kerreffekt bei hohen Drucken im Übergangsgebiet Gasförmig-flüssig," Berlin, 1940.
[22] Breazeale, *Phys. Rev.*, 1936, **49**, 625.
[23] Stuart, "Die Struktur des Freien Moleküls," Springer, Berlin, 1952, pp. 162 and 172.

C=C and the C–Cl links. If we write $b_1 = 2b_L^{C-Cl} \cos^2 \rho + 2b_T^{C-Cl} \sin^2 \rho + b_T^{C=C} + 2b_L^{C-H}$, where $b_1 = 0{\cdot}779_5 \times 10^{-23}$, we obtain ρ as 45° 44′, θ as 27° 8½′, and ϕ as 51° 40′, while the azimuthal angle between the planes of the C=C–Cl units is 66° 20′. That these angles are more suitable than those deduced by geometry can be seen from the facts that they lead to a Cl–Cl separation of $3{\cdot}5_3$ Å (against 3·7 Å reported [14]) and a $b_{2\,calc.}$ of $0{\cdot}947 \times 10^{-23}$ (against $0{\cdot}946 \times 10^{-23}$ found); b_2 is assumed to be situated parallel to the Cl–Cl direction. By difference (Table 4), b_3 is $0{\cdot}606_5 \times 10^{-23}$ (against $0{\cdot}608 \times 10^{-23}$ found).

Further Reference to Tri- and Tetra-chloroethylenes.—One might suspect that if *cis*-dichloroethylene is non-planar, the tri- and tetra-chloro-derivatives would be so also, volume factors being presumably responsible. It is therefore relevant to mention that application of the bond lengths and angles listed by Allen and Sutton [14] to planar configurations of these molecules reveals permitted maximum Cl–Cl separations as follow: $3{\cdot}1_8$ Å for *cis*-dichloroethylene, $3{\cdot}2_4$ Å for trichloroethylene, and 3·60 Å for tetrachloroethylene. Since the minimum effective radius of combined chlorine is *ca.* 1·6 Å (Stuart [24] quotes it as 1·58 Å), there can be no objection to the assumption of flatness for the tri- and tetra-chloro-substances. Even so, the degree of non-planarity now inferred for *cis*-dichloroethylene appears excessive if steric causes are alone operative, and no satisfactory alternative explanation suggests itself. The same remarks could be made concerning Bastiansen and Hassel's conclusions [25] that in *o*-dichloro- and hexachloro-benzenes the halogens are bent out of the plane of the ring by 18° and 12° respectively.

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UNIVERSITY OF SYDNEY, N.S.W., AUSTRALIA. [*Received, September 19th*, 1958.]

[24] Stuart, *Z. phys. Chem.*, 1935, *B*, **27**, 350.
[25] Bastiansen and Hassel, *Acta Chem. Scand.*, 1947, **1**, 489.

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233. *Molecular Polarisability. Ellipsoids of Polarisability for Certain Fundamental Heterocycles.*

By (MRS.) C. G. LE FÈVRE, R. J. W. LE FÈVRE, B. PURNACHANDRA RAO, and M. R. SMITH.

From the depolarisation factors for light scattered by solutions of pyridine, quinoline, *iso*quinoline, furan, thiophen, and pyrrole in carbon tetrachloride, together with electric double refraction and other measurements on the same systems, the molecular polarisability ellipsoids for these six solutes are specified. With the 5-ring structures a positive exaltation in polarisability is indicated only in the 2 : 5 (or 3 : 4) directions. Practical new data for pyridine, quinoline, and *iso*quinoline are supplied, but no essential alteration of earlier conclusions is necessitated.

THE polarisability ellipsoids for pyridine, quinoline, and *iso*quinoline published by Le Fèvre and Le Fèvre [1] were derived by making assumptions concerning the "anisotropy" terms [2] incorporated in their respective molar Kerr constants. For pyridine and quinoline, light-scattering observations on the vapours were used to calculate θ_1, while for *iso*quinoline (for which there were no such data) an approximation drawn from molecular dimensions was used. It has since been demonstrated [3] that with molar Kerr constants ${}_\infty({}_mK_2)$ measured at infinite dilution in carbon tetrachloride neither procedure is correct: the light scattering should be studied in the same solvent as that in which ${}_\infty({}_mK_2)$ is determined. This has now been done, with results as given below. Additionally, furan, thiophen, and pyrrole are now examined for the first time.

[1] Le Fèvre and Le Fèvre, *J.*, 1955, 2750.
[2] *Idem, Rev. Pure Appl. Chem.*, 1955, **5**, 261.
[3] Le Fèvre and Purnachandra Rao, *J.*, 1957, 3644.

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Experimental

Materials were purified as in refs. 1 and 3—6. Apparatus and methods have been described before (*e.g.*, refs. 2, 7, 8). Experimental observations are listed in Tables 1—3, and lead to the information in Table 4. The symbols follow the definitions given in refs. 1—3, and 7—9.

Table 1. *Electric double refractions of solutions in carbon tetrachloride * at 25°.*

Solute: Furan						
10^5w_2	658	2073	2115	2261	2398	3566
$10^7\Delta B$	0·004	0·016$_5$	0·017$_5$	0·018	0·020	0·029
whence $10^7\Delta B = 0{\cdot}778w_2 + 1{\cdot}21_5w_2^2$						
Solute: Thiophen						
10^5w_2	2141	4708	4821	6517	7566	8657
$10^7\Delta B$	0·026	0·056	0·057	0·070	0·082	0·102
whence $10^7\Delta B = 1{\cdot}16_7w_2 - 0{\cdot}38_5w_2^2$						
Solute: Pyrrole						
10^5w_2	621	909	1019	1515	1835	2981
$10^7\Delta B$	0·040	0·054	0·060	0·081	0·103	0·142
whence $10^7\Delta B = 6{\cdot}40_8w_2 - 54{\cdot}2w_2^2$						

* $B = 0{\cdot}070 \times 10^{-7}$ when $w_2 = 0$.

Table 2. *Depolarisation factors for solutions in carbon tetrachloride.**

Solute: Furan					
10^5f_2	3638	7771	11386	15031·5	18541
$10^2\Delta_{12}$	6·286	9·441	12·21	14·79	17·20
whence $\Delta\Delta_{12} = 0{\cdot}7981f_2 - 0{\cdot}302f_2^2$					
Solute: Thiophen					
10^5f_2	5225	7503	11250	15021	19625
$10^2\Delta_{12}$	6·850	8·331	10·62	12·85	15·84
whence $\Delta\Delta_{12} = 0{\cdot}6484f_2 - 0{\cdot}104f_2^2$					
Solute: Pyrrole					
10^5f_2	4485	9983	13647	18327·5	20834
$10^2\Delta_{12}$	6·815	10·35	13·12	16·65	17·24
whence $\Delta\Delta_{12} = 0{\cdot}7542f_2 - 0{\cdot}356f_2^2$					
Solute: Pyridine					
10^5f_2	3170	6548	8515	10293	16006
$10^2\Delta_{12}$	6·366	9·538	12·59	13·83	20·84
whence $\Delta\Delta_{12} = 0{\cdot}9106f_2 + 1{\cdot}106f_2^2$					
Solute: Quinoline					
10^5f_2	2168	4020	5952	9109	11895·5
$10^2\Delta_{12}$	7·627	11·08	14·38	20·48	25·97
whence $\Delta\Delta_{12} = 1{\cdot}844f_2 + 0{\cdot}358f_2^2$					
Solute: *iso*Quinoline					
10^5f_2	1747	3175	4745	6029	7518
$10^2\Delta_{12}$	8·122	12·03	16·21	19·70	23·96
whence $\Delta\Delta_{12} = 2{\cdot}647f_2 + 0{\cdot}982f_2^2$					

* $\Delta_1 = 0{\cdot}0346$ for $f_2 = 0$

[4] Buckingham, Chau, Freeman, Le Fèvre, Rao, and Tardif, *J.*, 1956, 1405.
[5] Harris, Le Fèvre, and Sullivan, *J.*, 1935, 1622.
[6] Buckingham, Harris, and Le Fèvre, *J.*, 1953, 1626.
[7] Le Fèvre and Le Fèvre, *J.*, 1953, 4041.
[8] Le Fèvre, "Dipole Moments," Methuen, London, 3rd edn., 1953, p. 45.
[9] Le Fèvre, Le Fèvre, and Oh, *Austral. J. Chem.*, 1957, **10**, 218.

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TABLE 3. *Dielectric polarisation and refraction measurements in carbon tetrachloride at 25°.*

10^5w_2 0	n_D^{25} ..... 1·4575	d_4^{25} ..... 1·58454	ε^{25} ..... 2·2270

Furan

10^5w_2	658	2073	2115	2261	2398	3566
n_D^{25}	1·4573	1·4564	14563	1·4562	1·4561	1·4553
d_4^{25}	1·58451	1·57720	1·56161	1·56060	1·55930	1·55780
ε^{25}	—	2·2544	2·2545	2·2551	2·2557	2·2714

whence $\Sigma\Delta n/\Sigma w_2 = -0{\cdot}057$; $\Sigma\Delta d/\Sigma w_2 = -1{\cdot}115$; $\Sigma\Delta\varepsilon/\Sigma w_2 = 1{\cdot}258$.

Thiophen

10^5w_2	156	2231	2671	4320	4821	5192	8657
n_D^{25}	—	—	1·4601	1·4617	1·4621	1·4624	1·4661
d^{25}	1·58332	1·56732	1·56388	—	—	1·54463	—
ε^{25}	2·2282	2·2441	2·2472	2·2602	—	2·2667	—

whence $\Sigma\Delta n/\Sigma w_2 = 0{\cdot}097$; $\Sigma\Delta d/\Sigma w_2 = -0{\cdot}771$; $\Sigma\Delta\varepsilon/\Sigma w_2 = 0{\cdot}765$.

Pyrrole

10^5w_2	621	909	1019	1515	1835	2981	3101
n_D^{25}	—	—	—	—	1·4595	1·4605	1·4608
d_4^{25}	1·57838	1·57557	1·57448	1·56953	—	—	—
ε^{25}	2·2842	2·3117	2·3210	2·3648	—	—	—

whence $\Sigma\Delta n/\Sigma w_2 = 0{\cdot}105$; $\Sigma\Delta d/\Sigma w_2 = -0{\cdot}989$; $\Sigma\Delta\varepsilon/\Sigma w_2 = 9{\cdot}19_5$.

TABLE 4. *Calculations of dipole moments, molar Kerr constants, polarisability semi-axes, etc., for solutes in carbon tetrachloride at 25°.*

	$\alpha\varepsilon_1$	β	γ	δ	$_\infty P_2$ (c.c.)	$_DP$ (c.c.)
Furan	$1{\cdot}25_8$	−0·708	−0·039	$11{\cdot}1_1$	30·4	19·6 [a]
Thiophen	0·765	−0·487	0·067	$16{\cdot}6_7$	29·7	23·8 [a]
Pyrrole	$9{\cdot}19_5$	−0·624	0·072	$91{\cdot}5_4$	85·3	20·8 [b]

	$_\infty(_mK_2) \times 10^{12}$	$(\theta_1 + \theta_2) \times 10^{35}$	$_\infty\delta_2^2 \times 10^3$	$_EP$ (c.c.)
Furan	$6{\cdot}2_6$	$1{\cdot}48_8$	$39{\cdot}7_0$	$18{\cdot}2_4$ [d]
Thiophen	$11{\cdot}1_9$	$2{\cdot}66_1$	$32{\cdot}4_9$	$22{\cdot}7_0$ [d]
Pyrrole	$44{\cdot}5_9$	$10{\cdot}6_9$	$37{\cdot}6_7$	$20{\cdot}0_3$ [d]
Pyridine	150·0 [c]	$35{\cdot}6_7$	$44{\cdot}8_9$	$23{\cdot}2_0$ [d]
Quinoline	149·1 [c]	$35{\cdot}4_8$	$88{\cdot}4_1$	$39{\cdot}6_0$ [d]
*iso*Quinoline	571·7 [c]	$135{\cdot}9_5$	126·4	$39{\cdot}4_0$ [d]

	$(b_1 + b_2 + b_3) \times 10^{23}$	$\theta_1 \times 10^{35}$	μ (D)	$10^{23}b_1$	$10^{23}b_2$	$10^{23}b_3$
Furan	$2{\cdot}16_9$	$1{\cdot}08_4$	0·72	$0{\cdot}74_3$	$0{\cdot}88_9$	$0{\cdot}53_7$
Thiophen	$2{\cdot}69_9$	$1{\cdot}34_{25}$	0·54	$1{\cdot}01_5$	$1{\cdot}01_4$	$0{\cdot}67_0$
Pyrrole	$2{\cdot}38_2$	$1{\cdot}19_9$	1·78	$0{\cdot}86_9$	$0{\cdot}93_2$	$0{\cdot}57_9$
Pyridine	$2{\cdot}75_9$	$2{\cdot}03_0$	2·37 [c]	$1{\cdot}07_2$	$1{\cdot}04_3$	$0{\cdot}64_5$
Quinoline	$4{\cdot}70_9$	11·65	2·27 [c]	1·68.	$2{\cdot}07_4$	$0{\cdot}94_9$
*iso*Quinoline	$4{\cdot}68_5$	16·49	2·65 [c]	1·96	$1{\cdot}91_4$	$0{\cdot}77_8$

[a] From ref. 5. [b] From ref. 6. [c] From ref. 1. [d] Extrapolated from refractions given in Landolt and Börnstein's "Tabellen," 1912 Edn., p. 1027. [e] From ref. 4.

DISCUSSION

Pyridine, Quinoline, and iso*Quinoline.*—Values of θ_1 calculated from observations on solutions are smaller than those derived from the depolarisation factors of the gases, or from alternatives based on scale-drawings [1] (Table 5). As expected,[1] the magnitudes of b_1 are little changed by the use of the correct θ_1 but b_2 and b_3 are more affected.

Furan, Thiophen, and Pyrrole.—The dielectric polarisations of these solutes in carbon tetrachloride have not been previously recorded. The values now found for their dipole moments (0·72, 0·54, and 1·78 D) agree with those ($0{\cdot}71_5 \pm 0{\cdot}02$, $0{\cdot}52 \pm 0{\cdot}05$, and

1·80 ± 0·07) determined earlier [5,6] in benzene. Marinangeli [10] has since given $\mu = 1{\cdot}74$ D for pyrrole in benzene.

Ingold [11] has drawn attention to the fact that the mean polarisabilities of these three heterocycles show negative exaltations, thiophen more markedly than furan or pyrrole. Since the semi-axes of the bond ellipsoids are now available for the C–H,[12] C–O,[13] C–C,[14] C–N,[15] N–H,[15] and C=C [16] links, the question as to whether the exaltation is a directional property can be investigated *a priori*. No measurements are yet to hand regarding the

TABLE 5. *Effects of different* θ_1 *values on the semi-axes calculated therewith.*

	Source of θ_1	$10^{23}\theta_1$	$10^{23}b_1$	$10^{23}b_2$	$10^{23}b_3$
Pyridine	$\propto \delta_2^2$	2·03	1·07	1·04	$0{\cdot}64_5$
,,	Δ_{gas}	3·54	1·06	1·13	0·55
,,	Shape factors	4·08	1·06	$1{\cdot}15_5$	0·53
Quinoline	$\propto \delta_2^2$	$11{\cdot}6_5$	1·69	2·07	0·95
,,	Δ_{gas}	18·8	1·65	2·24	$0{\cdot}79_5$
,,	Shape factors	21·0	1·64	2·29	0·76
*iso*Quinoline *	$\propto \delta_2^2$	16·5	1·99	1·91	0·78
,,	Shape factors	17·2	2·00	1·91	0·75

* No Δ_{gas} value available.

C–S bond, but for an inter-centre distance of 1·8 Å, b_L^{C-S} should [17] be *ca.* $0{\cdot}11 \times 10^{-23}$, so that, Vogel's [18] bond refractions being used, b_T^{C-S} appears as *ca.* $0{\cdot}22 \times 10^{-23}$ c.c.

As a preliminary it may be noted that with $b_L^{C-C} = 0{\cdot}098_6$, $b_T^{C-C} = 0{\cdot}027_4$, $b_L^{C=C} = 0{\cdot}280$, $b_T^{C=C} = 0{\cdot}077$, $b_V^{C=C} = 0{\cdot}073$, and $b_l^{C-H} = 0{\cdot}064$ (all $\times 10^{-23}$ c.c.), the calculated molecular semi-axes for benzene on a regular hexagonal model are: $10^{23}b_1 = 10^{23}b_2 = 1{\cdot}11$; $10^{23}b_3 = 0{\cdot}68_5$. The corresponding found values are: $10^{23}b_1 = 10^{23}b_2 = 1{\cdot}11$; $10^{23}b_3 = 0{\cdot}73$. The near-agreement between these sets justifies similar calculations for furan, thiophen, and pyrrole. Using $b_L^{C-O} = 0{\cdot}081$, $b_T^{C-O} = 0{\cdot}039$, $b_L^{C-N} = 0{\cdot}057$, $b_T^{C-N} = 0{\cdot}069$, $b_L^{N-H} = 0{\cdot}050$, $b_T^{N-H} = 0{\cdot}083$ and b's for other bonds as above, in conjunction with the valence angles given by Allen and Sutton,[19] we forecast semi-axes as follow:

		$10^{23}b_1$	$10^{23}b_2$	$10^{23}b_3$
Furan	calc.	0·92	0·67	$0{\cdot}51_5$
	obs.	0·74	0·89	0·54
	obs. – calc.	−0·18	+0·22	$+0{\cdot}02_5$
Thiophen	calc.	1·11	0·89	0·88
	obs.	$1{\cdot}01_5$	1·01	0·67
	obs. – calc.	$-0{\cdot}09_5$	+0·12	−0·21
Pyrrole	calc.	0·98	0·75	0·67
	obs.	0·87	0·93	0·58
	obs. – calc.	−0·11	+0·18	−0·09

In all three cases exaltations are predicted as positive in the b_2 direction, and as negative along b_1. On the estimates just quoted, exaltations of mean polarisabilities should be most negative for thiophen, less so for pyrrole, and a little positive for furan and benzene. The change in algebraic sign is contrary to experience, since benzene and furan actually exhibit small negative exaltations (ref. 11, p. 184). Numerically however the discrepancies are slight; they are probably due to minor errors in the bond and geometrical data used for prediction.

[10] Marinangeli, *Ann. Chim.* (*Italy*), 1954, **44**, 211, 219.
[11] Ingold, "Structure and Mechanism in Organic Chemistry," Cornell Univ. Press, New York, 1953.
[12] Le Fèvre and Le Fèvre, *Chem. and Ind.*, 1955, 1121.
[13] *Idem*, *J.*, 1956, 3549.
[14] *Idem*, *Chem. and Ind.*, 1956, 54.
[15] Aroney and Le Fèvre, *J.*, 1958, 3002.
[16] Bramley, Le Fèvre, Le Fèvre, and Rao, preceding paper.
[17] Le Fèvre, *Proc. Chem. Soc.*, 1958, 283.
[18] Vogel, *J.*, 1952, 514.
[19] Allen and Sutton, *Acta Cryst.*, 1950, **3**, 46.

It is noteworthy that this work reveals one more point of resemblance between benzene and thiophen: the ratios of their semi-axes of polarisability are practically the same (1·52 : 1·52 : 1, and $1{\cdot}51_5 : 1{\cdot}51_3 : 1$ respectively).

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UNIVERSITY OF SYDNEY, N.S.W., AUSTRALIA. [*Received, September 29th*, 1958.]

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234. *Studies in the Pyrolysis of Organic Bromides. Part XII.* The Unimolecular Decompositions of Ethyl Bromide and 4-Bromopent-1-ene.*

By P. J. THOMAS.

The thermal gas-phase decompositions of ethyl bromide and 4-bromopent-1-ene in the presence of olefinic inhibitors are homogeneous first-order reactions, the rate constants k_1 being $2{\cdot}8 \times 10^{13} \exp(-53{,}900/RT)$ sec.$^{-1}$ for EtBr and $8{\cdot}71 \times 10^{12} \exp(-44{,}700/RT)$ sec.$^{-1}$ for C_5H_9Br. In both cases the mechanism is the unimolecular elimination of hydrogen bromide. The results are discussed in relation to previous work on the decomposition of alkyl bromides.

THE thermal decomposition of ethyl bromide has been extensively studied by Daniels and his co-workers. In a recent publication [1] in which previous work is reviewed, the normal decomposition is shown to be a chain reaction. Daniels and Goldberg conclude that the reaction chains are initiated by bromine atoms produced by the reactions $C_2H_5Br + HBr \longrightarrow CH_3{\cdot}CH_3 + Br_2$; $Br_2 \longrightarrow Br + Br$, the hydrogen bromide being formed in the first instance by the molecular decomposition of ethyl bromide: $C_2H_5Br \longrightarrow C_2H_4 + HBr$. The present investigation, completed before Daniels and Goldberg's publication, deals with the isolation of the molecular mode of decomposition, by studying the reaction in the presence of added olefinic inhibitors. Previous work on the decomposition of *n*-propyl and *n*-butyl bromides [2] suggested that two mechanisms occurred in the decomposition of ethyl bromide.

The decomposition of 4-bromopent-1-ene has been studied to determine the effect of a β-vinyl substituent on the rate of unimolecular elimination.

EXPERIMENTAL

A commercial sample of ethyl bromide was dried ($CaCl_2$) and carefully fractionated. The middle fractions of constant physical properties were retained, b. p. 38·6°/760 mm. (corr.), n_D^{25} 1·4222 (lit.,[3] b. p. 38·4°, n_D^{25} 1·4220). The 4-bromopent-1-ene, a gift from Dr. P. A. T. Hoye, was prepared by bromination of pent-4-en-2-ol with phosphorus tribromide in the presence of pyridine and had b. p. 116·50°/756 mm., 74°/150 mm., n_D^{25} 1·4580.[4] *cyclo*Hexene was purified as in Part V.[5]

The reactions were followed by measuring the rate of pressure increase in a static system, the technique and apparatus being essentially that previously described,[6,7] the bromides being admitted to the reaction vessel from a vapour reservoir. Olefinic inhibitors were stored in a

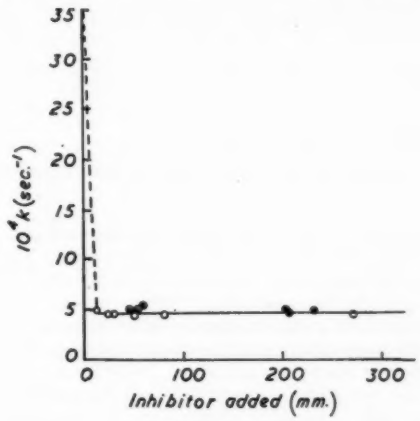
* Part XI, *J.*, 1958, 3016.

[1] Daniels and Goldberg, *J. Amer. Chem. Soc.*, 1957, **79**, 1314.
[2] Maccoll and Thomas, *J.*, 1957, 5033.
[3] Timmermans, "Physico-Chemical Constants of Pure Organic Compounds," Elsevier, Amsterdam, 1950.
[4] Hoye, Ph.D. Thesis, University of London, 1953.
[5] Green and Maccoll, *J.*, 1955, 2449.
[6] Maccoll, *J.*, 1955, 965.
[7] Maccoll and Thomas, *J.*, 1955, 979.

separate reservoir and, when required, were admitted to the reaction vessel before the bromides. No pre-mixing device was used.

Ethyl Bromide.—Although the investigation was primarily concerned with the effect of olefinic inhibitors, runs were carried out to ensure that Daniels and Veltman's results [8] could be reproduced in the present apparatus. In reaction vessels recently coated with a carbonaceous film by decomposition of allyl bromide, or in which inhibitors had been used, the reaction rate was irreproducible and invariably less than the rate previously reported. In a reaction vessel coated by the slow decomposition of the reaction products, a more reproducible reaction was observed. The initial first-order rate coefficient for an initial pressure of 360 mm. at 387° was $2{\cdot}8 \times 10^{-4}$ sec.$^{-1}$, to be compared with $3{\cdot}16 \times 10^{-4}$ sec.$^{-1}$ calculated from the rate equation reported by Daniels and Veltman.[8] The present value is lower, and induction periods were observed in all the pressure–time curves, in agreement with the later observation by Daniels and Goldberg.[1] The rate of decomposition was markedly reduced by added *cyclo*hexene. With increasing concentrations of *cyclo*hexene a limiting value was reached after which the rate became independent of the *cyclo*hexene concentration (Figure). The reaction was also inhibited by propene and by 2 : 4-dimethylpent-2-ene, the same limiting rate being observed as

Effect of inhibitors upon the rate of pyrolysis of ethyl bromide.
○, *cyclo*Hexene.
●, Propene.
◑, 2 : 4-Dimethylpent-2-ene.



with *cyclo*hexene. These two inhibitors are less efficient than *cyclo*hexene; a greater concentration was required to produce the same degree of inhibition. The residual reaction was thus shown to be independent of the concentration (above a certain limit) and nature of the olefinic inhibitor.

When the concentration of inhibitor was insufficient for complete inhibition, the observed kinetics were complex and characteristic of a partially inhibited decomposition of an alkyl bromide.[2] It was difficult to ascribe a significant value to a first-order rate constant in these circumstances and no points are included for the partially inhibited reaction in the Figure. In the region of partial inhibition, prolonged induction periods in the chain component make it possible to determine the rate-coefficient for the maximally inhibited reaction in the initial stages, although complete inhibition throughout the reaction is not attained. The value of k_1 in the presence of 60 mm. of propene was obtained in this manner.

The maximally inhibited decomposition was catalysed by clean glass surfaces, but the reaction was reproducible and homogeneous in reaction vessels coated with a thin film of carbonaceous material. The results of two series of experiments in a reaction vessel packed with glass tubing with a surface : volume ratio five times that of the empty vessel are included in Table 2. A definite increase in rate of the order of 15% was observed in the packed vessel but having regard to the large increase in the surface : volume ratio, it may be concluded that the heterogeneous component in the unpacked vessel is small and the reaction essentially homogeneous.

The maximally inhibited reaction is of the first order. The initial first-order rate

[8] Daniels and Veltman, *J. Chem. Phys.*, 1939, **7**, 757.

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coefficients, measured in a series of runs at 430° in an unpacked reaction vessel, are shown in Table 1, where p_1 is the concentration of *cyclo*hexene and p_0 the initial pressure of ethyl bromide.

TABLE 1. *Reaction at* 430°.

p_0 (mm.) ...	568	526	374	274	196	109	70	43	31	25
p_1 (mm.) ...	89	34	64	50	25	13	12	16	14	18
10^4k_1 (sec.$^{-1}$)	4·55	4·82	4·61	4·46	4·50	4·54	4·77	4·54	4·65	4·79

Mean value k_1 at 430° = 4·71 × 10^{-4} sec.$^{-1}$.

The rate coefficient k_1 shows no dependence on the initial pressure of ethyl bromide. In individual runs, the first-order character was maintained to about 50% of decomposition, after which the rate steadily diminished. This may have been due partly to the occurrence of the addition reactions $HBr + C_2H_4 \longrightarrow C_2H_5Br$ and $HBr + C_6H_{10} \longrightarrow C_6H_{11}Br$, and partly to the polymerisation of the ethylene formed. At 430° the first-order rate diminished after 40% of reaction and small quantities of non-condensable gases were formed in the later stages. The temperature range of the investigation was curtailed at 430° for this reason.

The temperature-dependence of the first-order rate constants was determined from the mean values for series of runs at different temperatures. The results are shown in Table 2. The rate constants can be expressed as $k_1 = 2{\cdot}8 \times 10^{13} \exp(-53{,}900/RT)$ sec.$^{-1}$.

TABLE 2.

Temp.	430°	416°p	414°	404·5°	398°	392°	385·5°p	382°
No. of runs ...	15	12	17	1	8	5	5	6
10^4k_1 (sec.$^{-1}$) ...	4·71	2·42(2·14)	1·84	1·06	0·75	0·52	0·39(0·34)	0·30

p = runs in packed vessel; figures in parentheses are interpolated values for k_1 in the unpacked vessel.

4-Bromopent-1-ene.—This compound decomposed at a measurable rate in the range 300—350°, accompanied by an overall pressure increase of about 80%. The reaction has been studied by measuring the rate of pressure increase, which has been interpreted on the basis of the reaction $C_5H_9Br \longrightarrow C_5H_8 + HBr$. It was verified analytically that the pressure increase (Δp) observed was a direct measure of the amount of hydrogen bromide formed. In a series of runs the contents of the reaction vessel were rapidly condensed into a trap cooled in liquid air.

TABLE 3.

p_0 (mm.)	206	208	210	217	209	204	107	112
Δp (mm.)	65	74	127	104	112	85	52	52
p_{HBr} anal. (mm.)	68	74	124	98	112	87	54	56

The mixture of reactant and products was then removed from the appparatus and the hydrogen bromide estimated by conventional methods. By carrying out similar determinations in which the reaction vessel was filled with known pressures of pure hydrogen bromide only, the analytical results could be related directly to the equivalent partial pressures of hydrogen bromide in the reaction vessel. The partial pressures of hydrogen bromide calculated from the analyses are compared in Table 3 with the total pressure change Δp immediately before condensation. Good agreement between the two methods was obtained. The elimination of hydrogen bromide from 4-bromopent-1-ene can result in the formation of one of two possible pentadienes, $CH_2{:}CH{\cdot}CH_2{\cdot}CH{:}CH_2$ or $CH_3{\cdot}CH{:}CH{\cdot}CH{:}CH_2$, but the composition was not determined.

The normal decomposition of 4-bromopent-1-ene indicated marked kinetic complexity and was not investigated in detail. The pressure–time curves for individual runs were sigmoid and the first-order rate coefficient increased rapidly as the reaction proceeded. The addition of small quantities of *cyclo*hexene did not affect the initial, but reduced the maximum rate of decomposition. Previous work [2] has shown that this behaviour is characteristic of a system in which a chain mechanism with a prolonged induction period is superimposed upon a molecular mechanism. With increasing pressures of *cyclo*hexene the maximum rate of decomposition was reduced to a limiting value identical with that of the initial induction period in the normal reaction. A *cyclo*hexene : bromide concentration ratio of 2 : 3 was required to suppress the chain reaction entirely.

Only the maximally inhibited reaction was studied in detail. As with ethyl bromide,

additions of inhibitors, insufficient to produce complete inhibition throughout the reaction, nevertheless prolonged the induction period in the chain mechanism sufficiently to enable the initial first-order rate coefficients of the maximally inhibited reaction to be measured. The lack of dependence of the rate coefficients of this residual reaction on the *cyclo*hexene concentration is shown in Table 4. The decomposition was catalysed by clean glass surfaces but

TABLE 4.

p_0 (mm.)	158	150	157	158	150	147
p_i (mm.)	49	70	161	161	184	300
10^4k_1 (sec.$^{-1}$)	7·90	8·45	7·84	8·42	8·45	8·22
p_i/p_0	0·31	0·47	1·02	1·02	1·23	2·04

where the walls of the reaction vessel were coated with a thin carbonaceous film, either by the decomposition of the reaction products or by the decomposition of allyl bromide, the reaction rate was reduced and became more reproducible. The results of a series of experiments in a packed reaction vessel with a surface : volume ratio five times that of the empty vessel are shown in Table 6. No appreciable increase in rate was observed in the packed vessel and it may be concluded that the reaction is essentially homogeneous.

The reaction is of the first order. This was demonstrated by the linearity of the logarithmic plots for the first 50% of decomposition and by the independence of the initial, first-order rate-coefficients of the initial pressure (Table 5).

TABLE 5. *Reaction at* 336·5°.

p_0 (mm.)	218	158	150	147	124	120	97	54	51·6
p_i (mm.)	96	49	161	184	127	79	201	51	44
10^4k_1 (sec.$^{-1}$)	7·9	8·42	8·45	8·22	7·76	7·46	7·84	8·36	8·51

Mean k_1 at 336·5° = 8·08 × 10^{-4} sec.$^{-1}$.

The ratio of the final : initial pressure for the maximally inhibited reaction was *ca.* 1·8. This will be partly due to equilibria being established between hydrogen bromide and the olefinic products and also the *cyclo*hexene present.[5] The formation of small quantities of hydrogen or methane and the coloration of the products indicated that the later stages of the reaction are probably further complicated by the polymerisation of the olefinic products. The decrease in the first-order rate coefficient observed after 50% of reaction may be attributed to the same causes.

TABLE 6.

Temp.	349·5°	341·5°	337·3°	336·5°	335·5°	313·5°	301·5°
No. of runs	5	6	2	9	8p	4	6
10^4k_1 (sec.$^{-1}$)	16·7	10·0	8·37	8·08	7·71 (7·59)	1·70	0·85

p = packed reaction vessel. The figure in parentheses is the interpolated value for k_1 in the unpacked vessel.

The variation of the first-order rate coefficients with temperature is shown in Table 6, the rate constant being expressed by the equation $k_1 = 8·71 \times 10^{13} \exp(-44{,}700/\boldsymbol{RT})$ sec.$^{-1}$, which is to be compared with the Arrhenius equation for the unimolecular decomposition of *sec.*-butyl bromide,[9] $k_1 = 3·39 \times 10^{13} \exp(-46{,}370/\boldsymbol{RT})$ sec.$^{-1}$.

DISCUSSION

The rates of thermal decomposition of ethyl bromide and 4-bromopent-1-ene have been shown to be reduced to a limiting value by added *cyclo*hexene. The maximally inhibited or residual reactions, which are independent of the *cyclo*hexene concentrations,

[9] Kale, Maccoll, and Thomas, *J.*, 1958, 3016.

have been characterised as homogeneous, first-order reactions involving the elimination of hydrogen bromide:

$$C_2H_5Br \longrightarrow C_2H_4 + HBr;\ E = 53{\cdot}9 \text{ kcal./mole}$$
$$C_5H_9Br \longrightarrow C_5H_8 + HBr;\ E = 44{\cdot}7 \text{ kcal./mole}$$

The frequency factor in both cases is *ca.* 10^{13} sec.$^{-1}$. The observed activation energies are too low for non-chain radical mechanisms to be involved and radical-chain mechanisms will be suppressed by the inhibitor present. It is concluded that the reactions proceed by the molecular splitting of hydrogen bromide, *i.e.*, the unimolecular elimination mechanism. This mechanism is consistent with the observed characteristics of the decompositions and is to be expected from previous studies of the thermal decomposition of related alkyl bromides.

Blades and Murphy [10] have reported an investigation of the decomposition of ethyl bromide by a flow technique with toluene as the carrier gas. Under these conditions any free-radical formation leads to the formation of dibenzyl. Dibenzyl was not detected in the products and Blades and Murphy concluded that the reaction proceeded by the unimolecular elimination of hydrogen bromide. The first-order rate constant was given by the equation

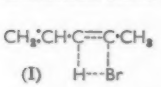
$$k_1 = 7{\cdot}3 \times 10^{12} \exp(-52{,}300/\boldsymbol{R}T) \text{ sec.}^{-1},$$

in good agreement with the present work. The temperature range was 527—626°, compared with 380—430° in this investigation.

The normal uninhibited decomposition of ethyl bromide has been fully discussed by Daniels and Goldberg.[1] The uninhibited decomposition of 4-bromopent-1-ene is complex and the chain mechanism of decomposition was considered unsuitable for a detailed investigation.

In 4-bromopent-1-ene, the β-methyl group in *sec.*-butyl bromide is replaced by a vinyl group. The Arrhenius equations for the unimolecular decompositions of these two compounds have been compared in the previous section. The relative rates of decomposition at 380° are $k_1(C_5H_9Br) : k_1(C_4H_9Br) = 1{\cdot}05 : 1$.

The decomposition of 4-bromopent-1-ene can occur in two ways, forming either penta-1 : 3- or penta-1 : 4-diene. The former involves elimination between the bromine atom and a hydrogen atom in the allylic position and the formation of a conjugated diene. Both factors would be expected to facilitate elimination if the rate-determining stage involved a transition state of the conventional four-centre type (I), in which the bonds are broken and formed simultaneously. The bond dissociation energy of the C–H bond at the 3-position should be considerably less than that of the corresponding bond in *sec.*-butyl bromide, and the hydrogen atom should be more easily removed. The transition state should also be stabilised by the conjugation which will develop between the forming double bond and the double bond already present. That neither of these factors leads to an increased rate of elimination from 4-bromopent-1-ene relative to *sec.*-butyl bromide indicates that the important rate-determining stage of the reaction is concerned solely with an activation of the C–Br bond. The breaking of the C–H bond and formation of the double bond occur in a later non-rate-determining stage.



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WILLIAM RAMSAY AND RALPH FORSTER LABORATORIES,
UNIVERSITY COLLEGE, LONDON, W.C.1. [*Received, October 17th*, 1958.]

[10] Blades and Murphy, *J. Amer. Chem. Soc.*, 1952, **74**, 6219.

235. *Studies in the Pyrolysis of Organic Bromides. Part XIII.*[1] *The Limiting Rate of Decomposition of* iso*Butyl Bromide in the Presence of Inhibitors.*

By G. D. Harden and Allan Maccoll.

Whereas *iso*butyl bromide normally decomposes by a mechanism involving radical-chains, the introduction of olefinic inhibitors reduces the rate to a limiting value, independent of the nature of the inhibitor. The first-order rate over the range 360—420° is given by $k_1 = 1{\cdot}12 \times 10^{13} \exp(-50{,}400/\boldsymbol{R}T)$ sec.$^{-1}$. The reaction occurring at maximal inhibition is the homogeneous, unimolecular elimination of HBr to form *iso*butene.

By analogy with other bromides containing a primary C–Br bond (Parts XII,[1] II,[2] and X[3]) it might be expected that *iso*butyl bromide would pyrolyse to yield *iso*butene and hydrogen bromide by a radical-chain mechanism. In the case of ethyl[1] and *n*-propyl and *n*-butyl[3] bromides, elimination of the chain component of the reaction isolated the unimolecular dehydrobromination. We now study the latter mechanism for *iso*butyl bromide.

Experimental and Results

*iso*Butyl bromide, prepared from *iso*butanol by the red phosphorus–bromine method, was washed with water, concentrated hydrochloric acid, water, 10% potassium carbonate solution, and water, dried ($CaCl_2$), and fractionally distilled, b. p. 91·35°/762·4 mm., n_D^{25} 1·4338 (Timmermans[4] gives b. p. 91·40°/760 mm., n_D^{25} 1·4340). A good commercial sample of *iso*butyl bromide, purified in the same way, gave results consistent with those obtained with the prepared material.

Preliminary runs in a seasoned vessel at 353° gave pressure–time curves of definitely sigmoid character, which suggested that a radical-chain mechanism was involved. Addition of *cyclo*hexene reduced the rate by a factor of about ten, indicating that at this temperature the radical-chain mechanism predominates. The radical-chain mechanism has not yet been exhaustively studied, and will not be considered here.

The apparatus and technique employed were essentially those described in Part I,[5] the rate of elimination being measured by the rate of pressure increase at constant volume. The stoicheiometry $C_4H_9Br \longrightarrow C_4H_8 + HBr$ was not checked by comparison of the HBr produced with the pressure increase. As mentioned in Part VI,[5] hydrogen bromide adds rapidly to *iso*butene in the absence of oxygen to form *tert.*-butyl bromide. Hence the HBr found analytically is much less than that estimated from manometric measurements, and the end point moves slowly in the direction of increasing HBr, owing to the hydrolysis of *tert.*-butyl bromide. However, the final pressure increase measured in a number of instances was found to be only slightly less than the initial pressure of the bromide. An analysis by Allen[7] for the dead-space correction shows that for an apparatus of the type used, if the theoretical value of p_t/p_0 is 2, then the measured value will be about 1·9. Values of p_t/p_0 (Table 1) show that the pressure approximately doubles during the course of a run, which is consistent with the overall reaction's being that suggested.

To determine the order of the reaction, a series of runs was done at 421·2° and rate coefficients corresponding to kinetics of order 0·5, 1, and 1·5 were derived. In no case were good straight lines obtained, but the constancy of the first-order coefficients over a wide range of initial pressures strongly suggests the first-order character of the reaction, at least in the early

[1] Part XII, preceding paper. A preliminary report of the Arrhenius parameters recorded here was given in *J. Chem. Phys.*, 1953, **21**, 178.
[2] Agius and Maccoll, *J.*, 1955, 973.
[3] Maccoll and Thomas, *J.*, 1957, 5033.
[4] Timmermans, "Physico-Chemical Constants of Pure Organic Compounds," Elsevier, Amsterdam, 1950.
[5] Maccoll, *J.*, 1955, 965.
[6] Harden and Maccoll, *J.*, 1955, 2454.
[7] Allen, *J. Amer. Chem. Soc.*, 1934, **56**, 2053.

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stages. The first-order rate constants are shown in Table 2, p_i being the pressure of *cyclo*hexene. They increased as the reaction proceeded; this can reasonably be identified as incomplete inhibition, also noted in the inhibition of the decomposition of *n*-propyl bromide by propene,[3] where it was shown that although the rate tended to increase during a run, the rate curve at least had a common tangent to the maximally inhibited curve. Thus rate constants derived in the initial stages of a run are significant. The increasing rate effect was more serious at lower temperatures than at the higher.

TABLE 1.

Temp.	p_i (mm.)	p_o (mm.)	p_t (mm.)	p_t/p_o	Temp.	p_i (mm.)	p_o (mm.)	p_t (mm.)	p_t/p_o
416·0°	129	124	227	1·81	395·4°	110	122	219·5	1·80
416·0	136	172	310	1·80	394·6	82	149	267·5	1·80
416·0	132	160	289·5	1·83	393·4	120	144	266	1·85
409·9	127	140	253·5	1·81					

TABLE 2. *Reactions at* 421·2°.

p_i (mm.)	211	203	215	225	200·5	193	209	80	79
p_o (mm.)	262	238	181·5	180	159	140	138	102	65·5
10^4k_1 (sec.$^{-1}$)	16·81	16·35	16·35	17·35	15·20	15·36	15·59	17·12	15·28

To identify the limiting rate with that of unimolecular elimination, a criterion proposed by Smith and Hinshelwood [3] was employed. These authors suggested that if two or more inhibitors reduce the rate of a reaction to the same value, then this is evidence that the maximally inhibited rate is that of an internal rearrangement rather than of a modified chain reaction. Since propene is a less efficient inhibitor than *cyclo*hexene [3] it was not tested, but *cyclo*hexene together with *cyclo*pentadiene and 2 : 4-dimethylpent-2-ene were used. Reproducible results could not be obtained with *cyclo*pentadiene, and this was presumed to be due to dimerisation of the inhibitor in the dead space. Values of the limiting rate obtained with 2 : 4-dimethylpent-2-ene are shown in Table 3, together with values of $k_{calc.}$ obtained from *cyclo*hexene-inhibited runs interpolated by use of the Arrhenius equation reported below. The results of Tables 2 and 3 confirm that the maximally inhibited reaction is unimolecular.

TABLE 3.

Temp. 386·6°	$k_{calc.} = 2·24 \times 10^{-4}$ sec.$^{-1}$		Temp. 388·4°	$k_{calc.} = 2·40 \times 10^{-4}$ sec.$^{-1}$	
p_i	p_o	10^4k_1 (sec.$^{-1}$)	p_i	p_o	10^4k_1 (sec.$^{-1}$)
201·5	168	2·93	224	170	2·57
144·5	128	2·54	235·5	147·4	2·53
142	114	2·31	249·5	140	2·30

No appreciable increase in rate was observed for a number of inhibited runs in a packed vessel of surface : volume ratio four times that of the unpacked vessel. The reaction is therefore homogeneous, which supports the conclusion of the last paragraph as to its nature.

TABLE 4.

No. of runs	Temp.	10^4k_1 (sec.$^{-1}$)	$10^4k_{calc.}$ (sec.$^{-1}$)	No. of runs	Temp.	10^4k_1 (sec.$^{-1}$)	$10^4k_{calc.}$ (sec.$^{-1}$)
7	411·9°	8·59	9·04	5	384·3°	2·08	1·93
6	402·2	5·12	5·45	5	371·0	0·854	0·855

TABLE 5.

No. of runs	12	3	9	8	8	2	6
Temp.	421·4°	420·9°	417·5°	411·7°	401·8°	401·6°	394·3°
10^4k_1 (sec.$^{-1}$)	16·02	16·32	12·11	9·60	5·00	5·75	3·46
No. of runs	5	5	6	5	6	6	
Temp.	391·4°	387·3°	386·6°	376·6°	366·0°	363·1°	
10^4k_1 (sec.$^{-1}$)	2·96	2·28	2·45	1·34	0·628	0·493	

Rates in the unpacked vessel are in Table 5. In view of the lack of dependence of the rate upon either the initial pressure of *iso*butyl bromide or of *cyclo*hexene, these have been grouped

[3] Smith and Hinshelwood, *Proc. Roy. Soc.*, 1942, *A*, **180**, 237.

together according to temperature. The rate can be expressed as $k_1 = 10^{13\cdot05} \exp(-50{,}400/RT)$ sec.$^{-1}$. In the Arrhenius plot, the scatter of the points about the best straight line was wider than usual, no doubt owing to the difficulty of producing complete inhibition.

Discussion

By the use of two different inhibitors a homogeneous, first-order decomposition of *iso*butyl bromide into *iso*butene and HBr, identified as an intramolecular elimination, has been isolated. The parameters of the rate equation are compared with those of previously studied bromides containing primary C–Br bonds in Table 6. The close similarity of the Arrhenius parameters for *n*-propyl, *n*-butyl, and *iso*butyl bromide decompositions confirms the proposed interpretations of the results.

Table 6.

Bromide	$10^{-13}A$ (sec.$^{-1}$)	E (kcal./mole)	Part
Ethyl	2·8	53·9	XII
n-Propyl	0·8	50·7	X
n-Butyl	1·5	50·9	X
*iso*Butyl	1·1	50·4	This work

An examination of the relative rates of elimination in the series ethyl, *n*-propyl, and *iso*butyl bromides, in which the β-hydrogen atom concerned in the elimination is attached to a primary, secondary, and tertiary carbon atom respectively, reveals the relatively small influence of the carbon–hydrogen bond upon the rate. Thus the rate for ethyl bromide at 380° being taken as unity, the relative rates for *n*-propyl and *iso*butyl bromides are 3·5 and 6·5 respectively. Barton *et al.*[9] showed that (−)-menthyl chloride, which contains β-hydrogen atoms attached to both secondary and tertiary carbon atoms, undergoes homogeneous unimolecular elimination in the region of 430° and yields approximately a 3 : 1 ratio of *p*-menth-3-ene to *p*-menth-2-ene. Thus within a single molecule, elimination with a β-hydrogen atom attached to a tertiary carbon atom occurs about three times as fast as elimination with a β-hydrogen atom attached to a secondary carbon atom. This ratio is in fair agreement with the ratio of the rates of decomposition of *n*-propyl and *iso*butyl bromide.

The difficulty of producing complete inhibition throughout the whole reaction suggests long chains in the uninhibited decomposition. Indeed there is evidence that along the series $CH_3{\cdot}CH_2Br$, $CH_3{\cdot}CH_2{\cdot}CH_2Br$, and $(CH_3)_2CH{\cdot}CH_2Br$ the chain length increases. If this is considered together with the observation [6,10] that there is no appreciable chain component in the pyrolysis of a bromide where the bromine atom is attached to a secondary or tertiary carbon atom, two generalisations regarding the occurrence or non-occurrence of a chain mode of decomposition in bromide pyrolysis can be made. First, for a chain decomposition to occur, the bromine atom to be eliminated must be attached to a primary carbon atom. Secondly, the chain length will increase as the β-hydrogen atom concerned in the elimination changes from CH_3- to CH_2- to $CH-$. Preliminary evidence [11] suggests that phenethyl bromide decomposes, in the absence of inhibitors, by a chain mechanism, which is further confirmation of the chain mechanism's being favoured by a weak β-carbon–hydrogen bond.

After this work had been completed the uninhibited decomposition of *iso*butyl bromide was reported by Sergeev [12] who found the decomposition to follow kinetics of order 1·5, but the results were not very reproducible. Also, bromine was found to accelerate the

[9] Barton, Head, and Williams, *J.*, 1952, 453.
[10] Maccoll and Thomas, *J.*, 1955, 979, 2445; Green and Maccoll, *J.*, 1955, 2449; Harden, *J.*, 1957, 5024; Harden and Maccoll, *J.*, 1957, 5028.
[11] Stephenson, unpublished work.
[12] Sergeev, *Doklady Akad. Nauk S.S.S.R.*, 1956, **106**, 299.

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rate markedly, and propene to retard it slightly. The rate constants could be represented by the Arrhenius equation

$$k = 1{\cdot}8 \times 10^6 \exp(-30{,}000/RT) \text{ mm.}^{-\frac{1}{2}} \text{ sec.}^{-1}$$

and Sergeev concludes that chains are generated on the wall of the reaction vessel. These observations are in essential accord with some made during the progress of the present investigation. Summarising the Russian work on *n*- and *iso*-propyl bromides [13] and the four butyl bromides,[12] Sergeev comes to essentially the conclusions reached here, namely that primary alkyl bromides decompose predominantly by a chain mechanism, whereas secondary and tertiary bromides decompose mainly by unimolecular elimination. In the next Part it will be shown that as the length of the alkyl chain increases in the straight-chain primary bromides, the chain component of the decomposition decreases relative to the unimolecular component.

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WILLIAM RAMSAY AND RALPH FORSTER LABORATORY,
UNIVERSITY COLLEGE, LONDON, W.C.1. [*Received, October 17th*, 1958.]

[13] Semenov, Sergeev, and Kapralova, *Doklady Akad. Nauk S.S.S.R.*, 1955, **105**, 301.

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236. *The Colour Isomerism and Structure of Some Copper Co-ordination Compounds. Part I. Absorption Spectra in Solution.*

By T. N. WATERS and D. HALL.

The absorption spectra of some copper(II) complexes of salicylaldehyde and 2-hydroxy-1-naphthaldehyde derivatives in pyridine, methanol, benzene, chloroform, and carbon tetrachloride have been obtained from 200 to 800 mμ. Measurements at 0°, 25°, and 43° gave no indication of a temperature effect, but significant differences were found on varying the solvents.

ONE of the unusual features of copper(II) co-ordination complexes is the existence of two differently coloured isomers of some compounds; *e.g.*, bis-(2-hydroxy-*N*-methyl-1-naphthaldimine)copper can be readily crystallised in either a green or a brown form.[1] Analysis and preliminary *X*-ray studies [2] have shown that the more obvious explanations involving solvent co-ordination, *cis–trans*-isomerism, and planar or tetrahedral ligand arrangements do not always apply. The suggestion that the isomers might arise from the use of inner and outer planar orbitals [3] can be criticised on the grounds that bonds involving two different orbital groups are unlikely in the same compound.[4] The results of a further investigation of some of these complexes by electronic absorption spectroscopy, magnetic susceptibility, and two *X*-ray diffraction analyses are presented in this and following papers.

Some qualitative observations gave the first indication of a possible explanation for the isomerism. It was noticed that both the green and the brown isomer of the above copper complex gave green solutions in pyridine and other co-ordinating solvents, and brown solutions in carbon tetrachloride. Similarly, *NN'*-disalicylidenepropane-1 : 2-diamine copper gave a green solution in pyridine and a violet solution in chloroform and methanol. Corresponding green and violet solids were isolated. The ethylenediamine analogue also gave green and violet solutions but could be prepared only as the green solid for reasons which became apparent after the *X*-ray studies had been completed. These similarities between the solutions and solids suggested that the colour of the green isomers

[1] Pfeiffer and Glaser, *J. prakt. Chem.*, 1938, **151**, 134; 1939, **153**, 265.
[2] von Stackelberg, *Z. anorg. Chem.*, 1947, **253**, 136.
[3] Ray and Sen, *J. Indian Chem. Soc.*, 1948, **25**, 473.
[4] Pauling, "Nature of the Chemical Bond," Cornell Univ. Press, New York, 1939.

was due to a five- or six-fold co-ordination of the copper atom in contrast to the violet or brown isomers where only four-fold co-ordination was indicated. A more detailed study of this correspondence was made by absorption spectroscopy on the solid compounds and solutions.

Experimental

The spectra of the solutions were obtained with a Beckman D.U. spectrophotometer fitted with thermospacers and a photo-multiplier unit. They were determined in the 200—800 mμ region, the range from 300 to 440 mμ being repeated with a lower solute concentration. Measurements were made at 43°, 25°, and 0° (all ±2°) on the copper complexes of the following: (I) salicylaldehyde, (II) 2-hydroxy-1-naphthaldehyde, (III) *NN'*-disalicylidene-ethylenediamine and (IV) -propane-1 : 2-diamine, (V) *NN'*-(2-hydroxy-1-naphthylidene)propane-1 : 2-diamine, (VI) *N*-methylsalicylaldimine, and (VII) 2-hydroxy-*N*-methyl-1-naphthaldimine. The solvents used were pyridine and benzene (both "AnalaR" grade, dried over $CaCl_2$), chloroform and carbon tetrachloride (both washed with water and twice distilled from $NaHSO_3$), and methanol (fractionally distilled, and redistilled from magnesium amalgam).

The complexes were prepared by the same general method.[5] Both (I) and (II) were made by mixing the free aldehyde with copper acetate in 50% aqueous methanol, the green product being filtered off, washed, and dried. Addition of free amine to the appropriate aldehyde complex suspended in 50% aqueous methanol gave the Schiff's base compounds; these were warmed, filtered off, dissolved in chloroform, and precipitated with ether. 2-Hydroxy-1-naphthaldehyde was prepared by the method of *Organic Syntheses*.[6] The coloured isomers were obtained by crystallising the complexes from various solvents or heating them to 140°.[1] All compounds have been described in the literature [1,5] except the green *form* of (IV) which was found to be a monohydrate and not a true isomer. The anhydrous violet compound is well known. The monohydrate was prepared by recrystallising the violet complex from damp methanol or dioxan and hand separating the resulting mixture of green and violet crystals [Found: C, 56·5; H, 4·3; N, 7·5; Cu, 17·5; H_2O (loss at 150°), 5·2. $C_{17}H_{16}O_2N_2Cu,H_2O$ requires C, 56·4; H, 5·0; N, 7·75; Cu, 17·6; H_2O, 5·0%]. A similar green isomer of (V) was also prepared. This became violet and lost weight when heated and was assumed to be the monohydrate. None of the other complexes lost weight at 150°.

Results and Discussion

A large number of spectra were obtained but only representative examples are shown to illustrate the conclusions drawn from them. It was found that the temperature effect, if any, was very small and less than the experimental errors arising from the slow evaporation of some solvents.

The spectra of the chloroform solution of each compound, obtained at 25°, are shown in Figs. 1—3. The heavy absorption in the 300—440 mμ region is ascribed to charge-transfer and free-ligand absorption, whereas the weak absorption in the visible region is ascribed to forbidden electronic transitions among the 3*d* levels of the copper atoms.[7,8] It is assumed that the absorption at *ca.* 570 mμ found in the complexes with an enforced *cis*-configuration arises from the unsymmetrical ligand fields expected in these compounds [cf. ligand-field calculations on *cis*- and *trans*-planar configurations in nickel(II) complexes [9]].

The effects of varying the solvents are shown in Figs. 4—6 for compounds (II), (V), and (VI). In the charge-transfer region these are best shown by (II), and in the visible region by (VI). Because of the possibility that evaporation of solvent had led to incorrect absorption coefficients, no account was taken of absolute peak heights; instead, their relative rise or fall was regarded as significant. In the charge-transfer region an increasing prominence of the absorption peak at approx. 380 mμ, relative to that at 310 mμ (probably

[5] Pfeiffer, Breith, Lubbe, and Tsumaki, *Annalen*, 1933, **503**, 84.
[6] *Org. Synth.*, 1942, **22**, 63.
[7] Calloman, Simpson, and Sheppard, *Ann. Reports*, 1955, **52**, 79.
[8] Orgel, *Quart. Rev.*, 1954, **8**, 422.
[9] Maki, *J. Chem. Phys.*, 1958, **28**, 651.

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FIGS. 1—3. *Spectra at 25° in chloroform.*

FIG. 1.

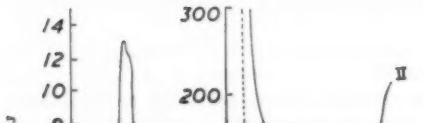


FIG. 2.

FIG. 3.

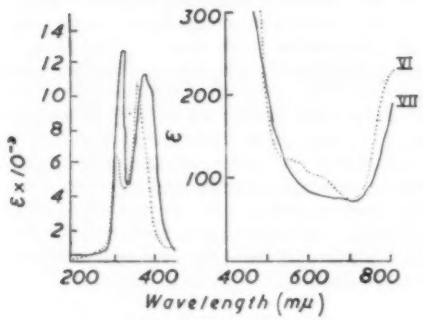
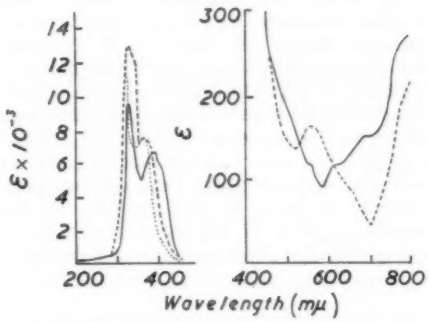
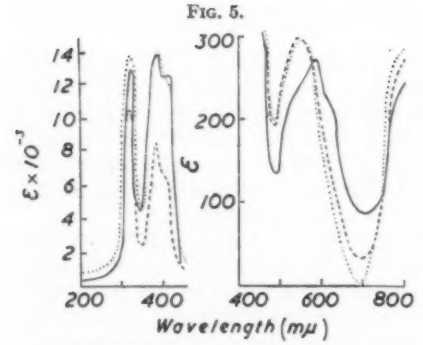


FIG. 4.



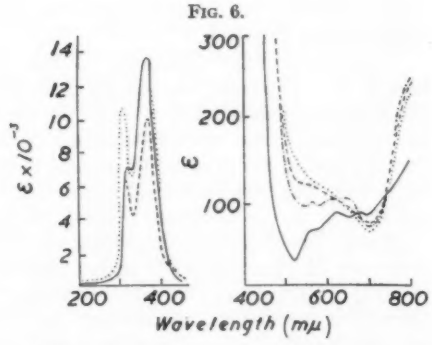
Compound (II): —— *in pyridine,* – – – – *in chloroform,* . . . . *in carbon tetrachloride.*

FIG. 5.



Compound (V): —— *in pyridine,* – – – – *in chloroform,* . . . . *in carbon tetrachloride.*

FIG. 6.



Compound (VI): —— *in pyridine,* – – – – *in chloroform,* . . . . *in carbon tetrachloride,* —·—·— *in methanol.*

due to free-ligand absorption [10]), resulted from an increase in the solvent co-ordinating power. This was taken as evidence of a new charge-transfer process arising from solvation to the metal. In the visible region a trough appeared at about 520 mμ and the existing one at 700 mμ was eliminated when the co-ordinating power of the solvent was increased. These spectral changes are consistent with the colour change from green in pyridine to violet or brown in carbon tetrachloride observed in solutions of these compounds. It is assumed that these effects are brought about by solvent co-ordination to the metal. It will be shown in Part II that a similar change in the visible region was found in the spectra of the solid compounds when two colour isomers were compared.

The variation of spectra with solvent follows the order, pyridine > methanol > chloroform ≈ benzene > carbon tetrachloride, which is almost certainly the order of the solvent co-ordinating power. As can be seen, both chloroform and benzene have some effect on the spectra, presumably through weak co-ordination to the copper. This is not unexpected in view of recent reports,[11] and the observation that some of these copper complexes will dissolve in chloroform but not in carbon tetrachloride. It follows that magnetic and spectral data obtained in benzene and chloroform solutions should be interpreted with regard for the fact that solvation may occur.

Although complex (III) was found to undergo the spectral changes indicative of solvation, it is known that the nickel analogue, unlike most salicylaldehyde–nickel complexes, gives the same spectrum in both chloroform and pyridine.[10] The solvation in the copper complex lends some support to the suggestion [10] that the nickel compound is also solvated but has retained the diamagnetic electron configuration of the parent compound.

CHEMISTRY DEPARTMENT, UNIVERSITY OF AUCKLAND, NEW ZEALAND.
[Present address (T. N. W.): CHEMISTRY DIVISION,
ATOMIC ENERGY RESEARCH ESTABLISHMENT, HARWELL,
BERKS, ENGLAND.] [*Received, September 22nd*, 1958.]

[10] Clark and Odell, *J.*, 1955, **3431**; 1955, **3435**; 1956, **520**.
[11] Reeves and Schneider, *Canad. J. Chem.*, 1957, **35**, 251; Fischer and Hafner, *Z. Naturforsch.*, 1955, **10**b, 665.

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237. *The Colour Isomerism and Structure of Some Copper Co-ordination Compounds. Part II.*[1] *Absorption Spectra of Solids.*

By T. N. WATERS and D. HALL.

The absorption spectra of some solid copper(II) complexes of salicylaldehyde and 2-hydroxy-1-naphthaldehyde derivatives have been obtained for potassium bromide discs. By analogy with the spectra in solution, it is suggested that the green complexes have a metal co-ordination number greater than the expected value of four.

IN Part I [1] a description was given of the electronic absorption spectra of some copper salicylaldehyde and 2-hydroxy-1-naphthaldehyde complexes in solution. The spectra of the solid compounds are now given for comparison.

Experimental.—Spectra were determined with a Beckman D.U. spectrophotometer fitted with a photomultiplier unit. The samples were pressed in potassium bromide discs,[2] 1 mg. of complex being mixed with 100 mg. of bromide. The agreement between the solid spectra and those previously obtained in solution [1] indicated that the absorption was little changed by side reactions with the bromide. However, the clear discs containing the samples slowly became opaque when exposed to radiation in the spectrophotometer, but as this effect also occurred with pure potassium bromide it could not be ascribed to a breakdown of the compounds. Because this fogging increased the optical density, accurate absorption coefficients were not

[1] Part I, Waters and Hall, preceding paper.
[2] Faust and Quagliano, *J. Amer. Chem. Soc.*, 1954, **76**, 5346.

obtained. The decrease in resolution available in the solid state also precluded the detection of the small changes in spectra found with the solutions. These difficulties were partially overcome as follows:

The effect of fogging, found by comparing the absorption of an opaque with a clear disc, of pure potassium bromide, added a constant value to the optical density throughout the measured range from 200 to 900 mμ. Discs judged to be equally fogged showed that all compounds had approximately the same optical density at 200 mμ—a result substantiated by measurements in solution—and this value was taken as an arbitrary zero. Because of the constant composition of the discs a comparison between spectra plotted in terms of optical density could then be made between compounds of similar molecular weight. To improve this comparison in the region of small absorption, and to counteract the lack of resolution, differential spectra were obtained by determining the optical density of one compound against another.

The preparation of the compounds has been described.[1]

Results and Discussion

Spectra in the 200—900 mμ region are shown in Figs. 1—3 for the copper complexes of the following compounds: (I) salicylaldehyde, (II) 2-hydroxy-1-naphthaldehyde, (III)

Fig. 1. Fig. 2. Fig. 3.

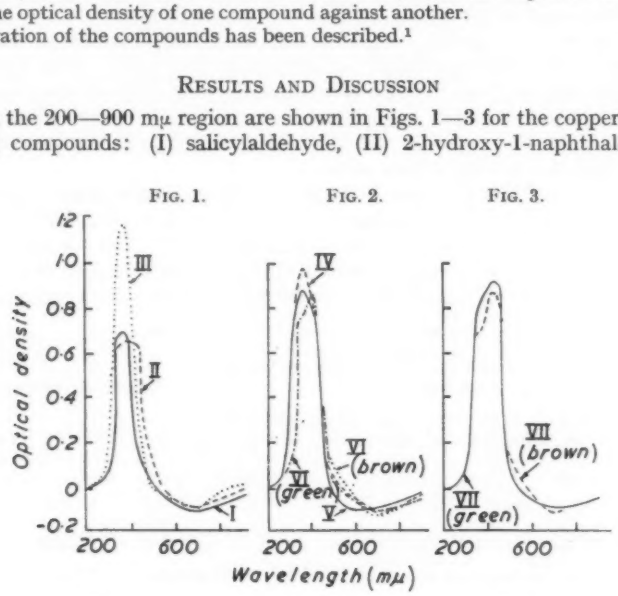
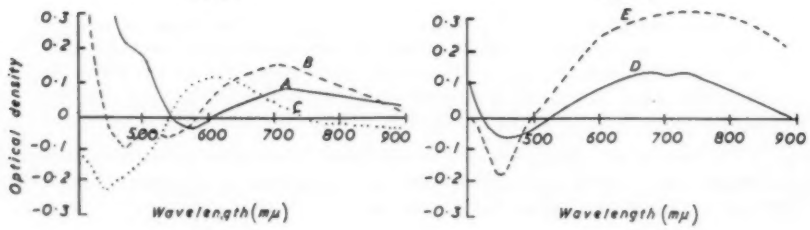


Fig. 4. Fig. 5.



NN'-disalicylidene-ethanediamine, (IV) *NN'*-disalicylidenepropane-1 : 2-diamine (violet), (V) monohydrate of (IV) (green), (VI) *N*-methylsalicylaldimine (green and brown isomers), (VII) 2-hydroxy-*N*-methyl-1-naphthaldimine (green and brown isomers).

Differential spectra obtained from 400 to 900 mμ are shown in Figs. 4 and 5 for the following pairs: (*A*) (III), against (V) as blank; (*B*) (III), against (IV) as blank; (*C*) (V), against (IV) as blank; (*D*) green isomer of (VI), against brown isomer of (VI) as blank; (*E*) green isomer of (VII) against brown isomer of (VII) as blank.

It is realised that the difficulties outlined above make interpretation doubtful but the

conclusions reached seem reasonable, and for the complexes of (III) and (V) have now been confirmed by *X*-ray diffraction studies.

In both solids and solutions there are large absorption peaks in the 300—450 mμ range and only small peaks elsewhere. These are respectively ascribed to charge-transfer and forbidden-transition processes. In the visible region there is a direct comparison between the solids, as shown by the differential spectra, and the solutions in various solvents. The green complexes absorb less at approx. 500 mμ and more at approx. 700 mμ than do the violet or brown compounds and in this respect correspond to the green solutions (solutions in co-ordinating solvents) which show a similar deviation from the violet or brown solutions (in non-co-ordinating solvents). The spectral change in solution has been ascribed to solvation,[1] giving five- or six-fold co-ordination of the copper atoms, and the above results suggest a similar effect in the solid state. If so, the green complexes have a co-ordination number greater than the four-covalency expected from the ligands, this value of four existing only in the violet or brown compounds.

The preliminary *X*-ray examination [3] of (VI), which shows that the green and the brown isomer have different crystal structures, supports this suggestion. The comparatively short copper–copper separation of 3·35 Å between the planar molecules of the green complex probably brings about the change in the spectrum by altering the ligand fields operating on the metal. Such an interaction between copper atoms must be weak, however, as the magnetic suceptibility is normal down to 81° K [4] (cf. anomalous magnetic susceptibility of copper acetate monohydrate,[5] where the copper–copper separation is only 2·64 Å [6]).

CHEMISTRY DEPARTMENT, UNIVERSITY OF AUCKLAND, NEW ZEALAND.
[Present address (T. N. W.): CHEMISTRY DIVISION,
ATOMIC ENERGY RESEARCH ESTABLISHMENT, HARWELL,
BERKS, ENGLAND.]

[*Received, September 22nd*, 1958.]

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[6] van Niekerk and Schoening, *Acta Cryst.*, 1953, **6**, 227.

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238. *Reaction of 2-Nitrofluorenone with Potassium Hydroxide, Aniline, and Sodium Anilide.*

By WILLIAM BRADLEY and F. P. WILLIAMS.

With potassium hydroxide in pyridine 2-nitrofluorenone gives 3-hydroxy-2-nitrofluorenone and a dicarboxylic acid of 4 : 4′-azoxydiphenyl. With aniline and potassium hydroxide the products are 6-hydroxyquinoxalino-[2,3-*a*]fluorenone and a 4-phenylazodiphenylcarboxylic acid. Sodium anilide at 20° gives the anil of 2-phenylazofluorenone, also prepared from 2-amino-fluorenone. At 40—45° sodium anilide gives two compounds $C_{24}H_{15}N_3$ and $C_{24}H_{15}ON_3$, considered to be the anils of 13-oxofluoreno[1,2-*b*]quinoxaline and a monoxide of this. 13-Oxofluoreno[2,3-*b*]quinoxaline was prepared for comparison. The mechanism of the reactions involved is discussed.

IN earlier publications [1,2] the direct replacement of hydrogen in nitrobenzene and α-nitronaphthalene by amines was described and the present is an extension of the work to 2-nitrofluorenone [3] (I).

On being heated with potassium hydroxide in " AnalaR " pyridine, the compound (I) gave 3-hydroxy-2-nitrofluorenone (II) (17%) and 4 : 4′-azoxydiphenyldicarboxylic acid (III). When a good laboratory grade of pyridine was used the main product isolated was

[1] Bradley and Robinson, *J.*, 1932, 1254.
[2] Bradley and Williams, *J.*, 1959, 360.
[3] Diels, *Ber.*, 1901, **34**, 1758.

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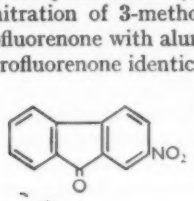
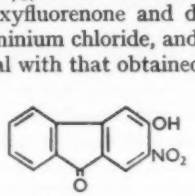
2 : 2′-azoxyfluorenone (20%). The constitution of the phenol (II) was established by (*a*) nitration of 3-methoxyfluorenone and demethylation of the resulting 3-methoxy-2-nitrofluorenone with aluminium chloride, and (*b*) methylation of the phenol to 3-methoxy-2-nitrofluorenone identical with that obtained in (*a*).



(I)



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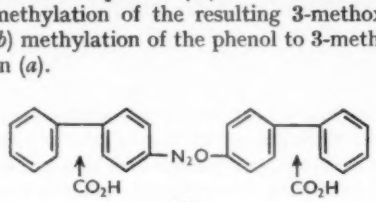
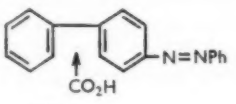


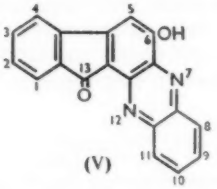
(III)

Under comparable conditions 2-nitrofluorene [4] was not hydroxylated by potassium hydroxide in pyridine. The effect of the carbonyl group of 2-nitrofluorenone in facilitating substitution by hydroxyl ions is analogous to other instances,[5,6] and in this case as in the others substitution occurs *para* to the carbonyl group.

With potassium hydroxide and aniline at 175—180° 2-nitrofluorenone gave a 4-phenylazodiphenylcarboxylic acid (IV) and 6-hydroxy-13-oxofluoreno[1,2-*b*]quinoxaline (V).



(IV)



(V)

The acid was identical with that obtained on heating 2-phenylazofluorenone with potassium hydroxide. The hydroxy-azine structure (V) rests on the following considerations. The compound forms an alkali-metal salt, a non-phenolic monomethyl ether, a cupric derivative, and a sulphate, $C_{19}H_{10}O_2N_2,H_2SO_4$. It is reduced with difficulty to an unstable, deeply coloured product. The boroacetic anhydride test was negative. It is identical with the derivative obtained on heating 2-*o*-nitroanilinofluorenone with potassium hydroxide in pyridine. In its behaviour on reduction it resembled 13-oxofluoreno[2,3-*b*]-quinoxaline (VI), prepared from 2 : 3-diaminofluorenone and *cyclo*hexane-1 : 2-dione with dehydrogenation of the tetrahydro-azine so formed with iodine.

With potassium hydroxide and aniline under reflux fluorenone gave diphenyl-2-carboxylic acid and fluorenone anil.

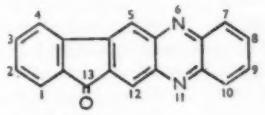
With sodium anilide in aniline at the room temperature 2-nitrofluorenone gave 2-phenylazofluorenone anil (VIII) and a small amount of the anil of (X).

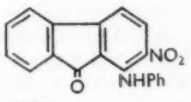
On hydrolysis, the anil (VIII) gave 2-phenylazofluorenone (IX) and aniline. The same compound (VIII) was also formed by the action of aniline and zinc chloride on 2-phenylazofluorenone, suggesting that in the reaction between 2-nitrofluorenone and sodium anilide 2-phenylazofluorenone is formed first and is then further converted into the anil. Fluorenone itself reacted with sodium anilide to form fluorenone anil identical with the compound prepared by condensation of aniline with fluorenone in the presence of zinc chloride.

With sodium anilide in aniline at 40—45° two compounds $C_{24}H_{15}N_3$ and $C_{24}H_{15}ON_3$ were formed, both of which gave aniline and 13-oxofluoreno[1,2-*b*]quinoxaline (X) on hydrolysis. The last resembled but was distinct from its isomer (VI). The compound $C_{24}H_{15}N_3$ was probably the anil of (X), and the compound $C_{24}H_{15}ON_3$ one of the two related oxides.

[4] *Org. Synth.*, Coll. Vol. II, p. 447.
[5] Bradley and Waller, *J.*, 1953, 3778.
[6] Backhouse and Bradley, *J.*, 1954, 4506.

It is clear from these results that the effect of potassium hydroxide alone, in the presence of pyridine, is to hydroxylate 2-nitrofluorenone in the 3-position and, in part, to open the fluorenone ring. In the presence of aniline, and without pyridine, a more complicated reaction ensues. The main result is conversion of the nitro-group into phenylazo, by reaction with aniline, accompanied by ring fission; at the same time a hydroxylated azine is formed. Separate experiments showed that the azine was not derived by the further action of alkali on 2-phenylazofluorenone. A more likely route to


(VI)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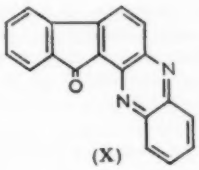
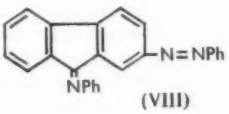
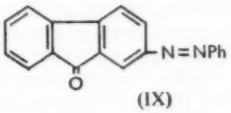

(X)


(VIII)


(IX)

its formation is the direct introduction of an anilino-group *ortho* to the nitro-group, giving (VII), followed by cyclisation to an azine and hydroxylation. This is the reaction involved in Wohl and Aue's synthesis of phenazine from nitrobenzene, aniline, and potassium hydroxide.[7] With sodium anilide in aniline at the room temperature the conversion of the nitro-group into phenylazo again occurs; at the same time a new reaction appears, conversion of the carbonyl group into an anil. At 40—45° the sodium anilide reaction is more complicated: anil formation occurs and at the same time the anilide ion substitutes the nucleus *ortho* to the nitro-group, and there is then cyclisation to an azine and its oxide.

Experimental

3-Hydroxy-2-nitrofluorenone.—3-Methoxyfluorenone [8] (3 g.) was refluxed for 4 hr. with aluminium chloride (5·7 g.) in chlorobenzene (100 ml.). The 3-hydroxy-derivative which was formed was purified by dissolution in 5% aqueous sodium hydroxide; on being recrystallised from chlorobenzene it afforded yellow needles, m. p. 227—228° (2·2 g.) (Ullmann [8] records m. p. 228—229°). Nitric acid (0·3 ml.; *d* 1·5) in glacial acetic acid (2 ml.) was added dropwise at 50—60° to a stirred suspension of finely divided 3-hydroxyfluorenone (1 g.) in acetic acid (20 ml.) and acetic anhydride (4 ml.). Stirring was continued for 30 min. and the solid which separated was crystallised from alcohol and then toluene. *3-Hydroxy-2-nitrofluorenone* forms pale yellow needles, m. p. 248—249° (Found: C, 64·9; H, 2·9; N, 5·9. $C_{13}H_7O_4N$ requires C, 64·7; H, 2·9; N, 5·8%). It dissolves in dilute aqueous potassium hydrogen carbonate with a yellow colour; the solution in concentrated sulphuric acid is orange-red. It sublimes readily under reduced pressure at 180—190°.

3-Methoxy-2-nitrofluorenone.—(*a*) Potassium hydroxide (0·2 g.) in methanol (2 ml.) was added to a solution of the above hydroxynitro-derivative (0·6 g.) in pyridine (5 ml.). An orange-yellow precipitate of the potassium salt was separated, dried, and then heated with methyl sulphate (7 ml.) at 100° for an hour. *3-Methoxy-2-nitrofluorenone* which separated on addition to water was crystallised from toluene and then chromatographed on alumina from chlorobenzene. Elution with toluene containing 1% of acetone gave greenish-yellow needles, m. p. 271—278° (Found: C, 66·4; H, 3·6; N, 5·1. $C_{14}H_9O_4N$ requires C, 65·9; H, 3·5; N, 5·5%), indistinguishable from the product obtained by nitration of 3-methoxyfluorenone.

(*b*) Finely ground 3-methoxyfluorenone (1 g.) was shaken for 12 hr. at the room temperature with nitric acid (10 ml.; *d* 1·42). The product obtained on addition to water was chromatographed on alumina from chlorobenzene and then crystallised from 95% alcohol, toluene, and

[7] Bradley and Leete, *J.*, 1951, 2136.
[8] Ullmann, *Ber.*, 1902, **35**, 4273.

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chlorobenzene in turn. 3-Methoxy-2-nitrofluorenone obtained in this way had m. p. 278—281° (Found: C, 66·4; H, 3·8; N, 5·1%). The products from (*a*) and (*b*) both gave reddish-pink solutions in concentrated sulphuric acid and the same absorption spectrum in " AnalaR " pyridine.

Action of Potassium Hydroxide on 2-Nitrofluorenone.—2-Nitrofluorenone (15 g.) and finely ground potassium hydroxide (13·2 g.) were refluxed with stirring in " AnalaR " pyridine (150 ml.). The colour of the reactants changed from yellow through dark red and deep green to brown. After 3 hr. the mixture was added to water and acidified, and the solid collected. This was dried (16·5 g.), powdered, and then extracted with cold 15% aqueous potassium hydrogen carbonate (2 × 150 ml.); a residue (2·7 g.) remained. Acidification of the filtered solution gave a brown solid (13·1 g.) which was dried and then sublimed *in vacuo* at 180—190°. A yellow crystalline sublimate (2·75 g.) was formed which crystallised from benzene in slender, pale yellow needles, m. p. 247—248° (Found: C, 64·8; H, 3·0; N, 5·6%), not depressed by 3-hydroxy-2-nitrofluorenone obtained by the nitration of the 3-hydroxy-derivative. The portion (8 g.) of the alkali-soluble material which did not sublime was extracted twice with 20% aqueous potassium hydrogen carbonate (100 ml.). The filtered extract gave yellow crystals on being kept and these were collected, acidified, and then crystallised from alcohol. Pale yellow needles (0·7 g.), m. p. 292—293° (Found: C, 71·4; H, 4·1; N, 6·8. $C_{26}H_{18}O_5N_2$ requires C, 71·4; H, 3·9; N, 6·4%), were obtained. The absorption spectrum in 95% alcohol showed the absence of typical fluorenone bands and a similarity to 4-phenylazodiphenyl-2(or 2′)-carboxylic acid. Reduction with stannous chloride in hydrochloric acid gave a primary amine.

There was no corresponding hydroxylation when 2-nitrofluorene was used instead of 2-nitrofluorenone in this experiment.

Fluorenone Anil.—A solution of sodium anilide was prepared by refluxing sodium (2·5 g.), copper bronze (0·05 g.), and nickel oxide (0·05 g.) in " AnalaR " aniline (65 ml.) until reaction ceased. The solution was cooled to 50° and a solution of fluorenone (4 g.) in " AnalaR " aniline (10 ml.) was added dropwise with stirring during 30 min. Dilute sodium hydroxide was added and the product obtained as a brown residue after distillation in steam. The acetone-soluble part was chromatographed on alumina from benzene. Elution with benzene–light petroleum (b. p. 60—80°) and recrystallisation from light petroleum (b. p. 40—60°) gave large yellow prisms, m. p. 86—87° (Found: C, 89·5; H, 5·0; N, 5·3. Calc. for $C_{19}H_{13}N$: C, 89·4; H, 5·3; N, 5·5%), which on being heated with aqueous-alcoholic hydrochloric acid gave fluorenone and aniline.

2-Phenylazofluorenone.—Nitrosobenzene (2·7 g.) and 2-aminofluorenone (5 g.) in acetic acid (10 ml.) were heated at 80° for 4 hr. The acid-insoluble portion of the product was chromatographed on alumina from chlorobenzene, the main zone eluted with toluene, and the *2-phenylazofluorenone* so obtained crystallised from benzene–ligroin as orange prisms, m. p. 159—160° (Found: C, 79·9; H, 3·9; N, 10·1. $C_{19}H_{12}ON_2$ requires C, 79·9; H, 4·2; N, 9·9%), which dissolved in concentrated sulphuric acid with an orange-brown colour. Reduction with stannous chloride and hydrochloric acid gave 2-aminofluorenone and aniline.

2-Phenylazo-9-phenyliminofluorene.—Aniline (0·5 ml.), 2-phenylazofluorenone (0·5 g.), and zinc chloride (0·05 g.) were heated at 170° for 30 min. and then added to water. The resulting suspension was made just alkaline, unchanged aniline was distilled in steam, and the residue chromatographed on alumina from benzene. The main zone was eluted with 95% alcohol, and the solid so obtained crystallised (0·4 g.) from benzene–light petroleum (b. p. 60—80°). *2-Phenylazo-9-phenyliminofluorene* forms orange-yellow prisms, m. p. 172—173° (Found: C, 83·4; H, 4·9; N, 11·7. $C_{25}H_{17}N_3$ requires C, 83·5; N, 4·7; N, 11·7%).

Hydrolysis. On being heated on a steam-bath for 10 min. with a mixture of 95% alcohol (3 ml.), water (1·5 ml.), and concentrated hydrochloric acid (1·5 ml.) the above anil (0·2 g.) gave 2-phenylazofluorenone and aniline.

2-o-Nitroanilinofluorenone.—(*a*) 2-Chlorofluorenone [9] (2 g.), *o*-nitroaniline (1·54 g.), potassium carbonate (1·3 g.), copper bronze (0·02 g.), and cupric acetate (0·06 g.) were refluxed in nitrobenzene (10 ml.) for 3 hr. After addition to water and steam-distillation a solid remained, and this was chromatographed on alumina from chlorobenzene. Elution of the main zone with 95% alcohol and concentration of the eluate gave *2-o-nitroanilinofluorenone* as orange-red needles (0·25 g.), m. p. 207—208° (Found: C, 71·8; H, 3·9; N, 8·9. $C_{19}H_{12}O_3N_2$ requires C,

[9] Courtot, *Compt. rend.*, 1927, **184**, 1179.

72·2; H, 3·9; N, 8·9%), which disolved in pyridine with a yellow colour rendered deep blue-violet on the addition of a drop of methanolic potassium hydroxide. (*b*) The same compound, m. p. 206—207° (Found: C, 71·8; H, 3·8; N, 8·8%), was obtained by refluxing 2-aminofluorenone (2 g.), *o*-chloronitrobenzene (1·9 g.), potassium carbonate (1 g.), copper bronze (0·01 g.), and cupric acetate (0·02 g.) in *o*-dichlorobenzene (15 ml.) for 10 hr.

13-*Oxofluoreno*[2,3-b]*quinoxaline and* 13-*Oxodibenzo*[f,h]*fluoreno*[2,3-b]*quinoxaline.*—2 : 3-Diaminofluorenone was prepared by Eckert's method [10] and obtained as brown prisms, m. p. 175—177° (Eckert [10] gives m. p. 185°) (Found: C, 74·6; H, 4·9; N, 13·3. Calc. for $C_{13}H_{10}ON_2$: C, 74·3; H, 4·8; N, 13·3%).

Solutions of the above diamine (0·2 g.) and phenanthraquinone (0·2 g.) in the minimum volume of acetic acid were mixed. A yellow precipitate was formed immediately and this was separated, chromatographed on alumina from chlorobenzene, eluted with toluene, and recovered, and the solid so obtained crystallised from 95% alcohol. Yellow crystals (0·3 g.) of 13-*oxodibenzo*[f,h]*fluoreno*[2,3-b]*quinoxaline*, m. p. 342—344° (Found: N, 7·4. $C_{27}H_{14}ON_2$ requires N, 7·3%), were obtained which dissolved in concentrated sulphuric acid with a red-violet colour. The *sulphate* formed orange-yellow needles (Found: N, 5·7. $C_{27}H_{16}O_5N_2S$ requires N, 5·8%).

13-*Oxofluoreno*[2,3-b]*quinoxaline.*—The above diamine (0·45 g.) and *cyclo*hexane-1 : 2-dione (0·25 g.) were refluxed for 2 hr. in acetic acid (15 ml.). The product was isolated as in the preceding preparation and 7 : 8 : 9 : 10-*tetrahydro*-13-*oxofluoreno*[2,3-b]*quinoxaline* obtained as straw-coloured needles (0·18 g.), m. p. 202—203° (Found: C, 79·9; H, 4·8; N, 9·7. $C_{19}H_{14}ON_2$ requires C, 79·7; H, 4·9; N, 9·8%), which gave an orange-red colour in concentrated sulphuric acid. Addition of zinc dust to the greenish-yellow solution in acetic acid caused a slow change to green and finally on being warmed to brownish-red. The tetrahydroazine (0·1 g.) was refluxed with iodine (0·35 g.) in acetic acid for 8 hr. The product was chromatographed on alumina from chlorobenzene, eluted with toluene, and crystallised first from 95% alcohol and then from benzene. 13-*Oxofluoreno*[2,3-b]*quinoxaline* was obtained (0·06 g.) as pale greenish-yellow needles, m. p. 239—241° (Found: C, 80·2; H, 3·2. $C_{19}H_{10}ON_2$ requires C, 80·8; H, 3·6%), which dissolved in concentrated sulphuric acid with a dark violet colour. On being heated with zinc in acetic acid the yellow solution changed through green to reddish-brown. The colour faded on cooling but was restored on heating.

Action of Sodium Anilide on 2-*Nitrofluorenone.*—(a) *At the room temperature.* Sodium anilide was prepared from sodium (7·5 g.), copper bronze (0·1 g.), nickel oxide (0·1 g.) and "AnalaR" aniline (190 ml.) under reflux in nitrogen until the metal had dissolved. The resulting solution was cooled to 15° and a suspension of 2-nitrofluorenone (15 g.) in "AnalaR" aniline (30 ml.) added in portions during 30 min. The colour changed through red to brown. After being stirred for 30 min. longer the solution was added to water and steam-distilled, and the acetone-soluble part of the black solid (24·5 g.) so obtained was chromatographed on alumina from benzene. One of the zones was orange in colour and this was eluted with benzene. Concentration of the benzene solution gave a solid and this was crystallised from benzene–ligroin, then from ligroin, and re-chromatographed on alumina from benzene. The main band, eluted and crystallised from benzene–light petroleum (b. p. 60—80°), gave 2-phenylazo-9-phenyliminofluorene, m. p. 171—172°, undepressed by the authentic compound. The two samples had the same absorption spectrum in 95% alcohol.

(b) *At* 45—50°. This experiment was identical with (a) except that the reaction temperature was 45—50°. Two orange zones were formed. The lower was eluted with benzene, the eluate was concentrated and light petroleum (b. p. 60—80°) added; orange-red needles (0·6 g.), m. p. 217—218° (Found: C, 83·1; H, 5·1; N, 11·1%) (product B), were obtained. The upper zone eluted with 95% alcohol afforded after concentration of the eluate orange-red needles (0·5 g.), m. p. 181—182° (Found: C, 79·8; H, 4·6; N, 11·1%) (product C).

Hydrolysis of B and C. Formation of 13-*oxofluoreno*[1,2-b]*quinoxaline.* A solution of product B (0·2 g.) in 95% alcohol (4 ml.), water (2 ml.), and concentrated hydrochloric acid (4 ml.) was heated on a steam-bath for 3 hr. Water (90 ml.) was then added and the precipitated solid collected; the filtrate contained a diazotisable amine. Crystallisation of the solid from benzene–light petroleum (b. p. 60—80°) gave pale yellow needles (0·12 g.), m. p. 276—277° (Found: C, 80·7; H, 3·5; N, 10·0. $C_{19}H_{10}ON_2$ requires C, 80·8; H, 3·6; N, 9·9%). 13-*Oxofluoreno*[1,2-b]*quinoxaline* gives a violet solution in concentrated sulphuric acid. On being

[10] Eckert, *J. prakt. Chem.*, 1928, **118**, 263.

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heated with zinc dust the yellow solution in acetic acid changed to green, and on being warmed to magenta. On cooling, the colour faded but was restored on heating.

Similar hydrolysis of product C (0·2 g.) gave again a diazotisable amine and the same yellow needles (0·12 g.), m. p. 276—277° (Found: C, 80·8; H, 3·5; N, 10·0%), as resulted from B. A mixture of the two products showed no m. p. depression.

Action of Aniline and Potassium Hydroxide on 2-Nitrofluorenone. Formation of 6-Hydroxy-13-oxofluoreno[1,2-b]*quinoxaline and 4-Phenylazodiphenyl-2(or 2′)-carboxylic Acid.*—Finely powdered potassium hydroxide (18·75 g.) was added in small successive amounts during 30 min. to a stirred solution of 2-nitrofluorenone (15 g.) in " AnalaR " aniline (80 ml.) at 175—180°. Stirring was continued for 30 min., then the resulting dark melt was cooled, added to water, and distilled in steam. The non-volatile product consisted of an alkali-insoluble residue (R) (8·3 g.) and a solution from which brown material (P) (7·7 g.) was precipitated after filtration and acidification. The residue (R) was first extracted hot with chlorobenzene and then alcohol and finally crystallised from acetic acid and then pyridine. Pale yellow needles, m. p. 303—304° (Found: C, 76·5; H, 3·5; N, 9·2. $C_{19}H_{10}O_2N_2$ requires C, 76·5; H, 3·4; N, 9·4%), were obtained. This *6-hydroxy-13-oxofluoreno*[1,2-b]*quinoxaline* formed a red sodium salt with alcoholic sodium sulphide but no reduction occurred even on heating. Addition of a solution of stannous chloride in concentrated hydrochloric acid to a solution in hot acetic acid changed the colour from yellow to magenta and finally to brown. No aniline was formed in this reaction and the original compound was recovered after the product had crystallised from chlorobenzene. It dissolved in concentrated hydrochloric with a dark orange colour and gave a violet solution in concentrated sulphuric acid. The boroacetic anhydride test was negative.

Addition of concentrated sulphuric acid (0·5 ml.) drop by drop to a solution of the 6-hydroxy-compound (0·4 g.) in hot acetic acid (150 ml.) precipitated orange-red prisms of a *sulphate* (Found: C, 57·3; H, 2·9; N, 6·6; S, 7·8. $C_{19}H_{10}O_2N_2,H_2SO_4$ requires C, 57·6; H, 3·0; N, 7·1; S, 8·1%) after concentration and cooling. The sulphate was hydrolysed on addition to water. It dissolved in concentrated sulphuric acid with a violet colour.

Solutions containing cupric acetate (0·25 g.) in pyridine (5 ml.) and the 6-hydroxy-compound (0·25 g.) in water (4 ml.) and pyridine (12 ml.) were mixed and refluxed for 3 hr. A brown solid separated on cooling and this was collected and washed with a solution of ammonium chloride in aqueous ammonia (Found: C, 69·5; H, 3·2; Cu, 8·7. $C_{38}H_{18}O_4N_4Cu$ requires C, 69·4; H, 2·7; Cu, 9·7%). On being dissolved in concentrated sulphuric acid and then added to water the *cupric derivative* gave the original 6-hydroxy-derivative, m. p. 302—303°.

Methyl toluene-*p*-sulphonate (1·0 g.) was added in 0·2 g. portions at intervals of 2 hr. to a refluxing solution of the 6-hydroxy-derivative (0·5 g.) in *o*-dichlorobenzene (20 ml.) containing anhydrous potassium carbonate (1·0 g.). Then refluxing was continued for 7 hr., the suspension was filtered, and the residue extracted with hot *o*-dichlorobenzene. The combined solutions were made up to 50 ml. with addition of more *o*-dichlorobenzene and then chromatographed on alumina. The main yellow zone was eluted with toluene containing acetone (1%) and the *6-methoxy-derivative* crystallised from benzene as pale yellow needles, m. p. 243—244° (Found: C, 77·25; H, 3·9; N, 8·6. $C_{20}H_{12}O_2N_2$ requires C, 76·9; H, 3·9; N, 9·0%). It did not form a salt with sodium hydroxide solution.

Preparation of 6-hydroxy-13-oxofluoreno[1,2-b]*quinoxaline from 2-o-nitroanilinofluorenone.* Potassium hydroxide (0·15 g.) and 2-*o*-nitroanilinofluorenone (0·15 g.) were ground together, refluxed in pyridine (4 ml.) for 36 hr. with stirring, and added to water. The solution was acidified, and the resulting precipitate was collected, dried, and sublimed at 0·01 mm. from a bath at 275—280°. The sublimate crystallised from chlorobenzene as pale yellow needles (0·07 g.), m. p. 302—303° (Found: C, 76·2; H, 3·7; N, 9·4%), which did not depress the m. p. of the authentic 6-hydroxy-compound.

4-Phenylazodiphenyl-2(or 2′)-carboxylic acid. The precipitate (P) obtained from the action of aniline and potassium hydroxide on 2-nitrofluorenone was stirred for 2 hr. with 20% aqueous potassium hydrogen carbonate (100 ml.). The bright orange solid formed was stirred with dilute hydrochloric acid, and the orange solid obtained crystallised from chlorobenzene as needles (2·5 g.), m. p. 204—205° (Found: C, 75·5; H, 4·7; N, 9·2. $C_{19}H_{14}O_2N_2$ requires C, 75·5; H, 4·6; N, 9·3%), of *4-phenylazodiphenyl-2(or 2′)-carboxylic acid.* This derivative gave a yellow solution in concentrated sulphuric acid. The ultraviolet absorption spectrum in 95% alcohol showed the absence of characteristic fluorenone bands. On being reduced with

stannous chloride (2 g.) in concentrated hydrochloric acid (5 ml.) and acetic acid (5 ml.) 4-phenylazodiphenyl-2(or 2′)-carboxylic acid (0·4 g.) gave aniline, characterised as 1-phenylazo-2-naphthol, m. p. and mixed m. p. 129—131°.

The carboxylic acid (0·4 g.) was refluxed for 4 hr. with 3% methanolic hydrogen chloride (10 ml.). The crystals which separated on cooling recrystallised from methanol as orange-yellow prisms, m. p. 70—71° (Found: C, 76·3; H, 4·8; N, 9·1. $C_{20}H_{16}O_2N_2$ requires C, 76·0; H, 5·1; N, 8·9%).

Action of Potassium Hydroxide in Aniline on 2-Phenylazofluorenone.—2-Phenylazofluorenone (3 g.) was intimately ground with potassium hydroxide (3 g.) and refluxed in "AnalaR" aniline (15 ml.) for 1 hr. with stirring. After being cooled the resulting suspension was added to water and acidified. The precipitate was dried and extracted with ligroin (b. p. 100—120°), and the filtered extract concentrated to yield crystals, m. p. 180—195° (0·14 g.). On being stirred for 2 hr. with 20% aqueous potassium carbonate (50 ml.) these gave a bright orange-yellow solid. This was treated with dilute hydrochloric acid, and the orange solid which was formed was crystallised from chlorobenzene to give prisms, m. p. 204—205° (Found: C, 74·8; H, 4·7; N, 9·0%), not depressed by the 2-phenylazodiphenylcarboxylic acid, m. p. 204—205°, obtained on reaction of aniline and potassium hydroxide with 2-nitrofluorenone.

3-Bromo-2-phenylazofluorenone.—2-Amino-3-bromofluorenone [11] (4 g.) in the minimum volume of acetic acid was stirred with nitrosobenzene (1·4 g.) in the same solvent (10 ml.) at 80—90° for 9 hr. After being crystallised from chlorobenzene, chromatographed on alumina, and crystallised from toluene *3-bromo-2-phenylazofluorenone* formed orange-yellow needles, m. p. 231—232° (Found: C, 62·5; H, 3·0; N, 7·7; Br, 22·3. $C_{19}H_{11}ON_3Br$ requires C, 62·8; H, 3·0; N, 7·7; Br, 22·0%). This derivative gave a reddish-orange solution in concentrated sulphuric acid.

2 : 2′-Azoxyfluorenone.—Zinc dust (10 g.) and a solution of calcium chloride (3·4 g.) in water (5 ml.) were added to a suspension of 2-nitrofluorenone (10 g.) in water (240 ml.) and alcohol (260 ml.). After being refluxed for 2 hr. the suspension was cooled and filtered, and the filtrate was concentrated to yield a further precipitate. The combined solids were dried and extracted with trichlorobenzene (500 ml.), and the solution so obtained was cooled. Yellow needles separated and were chromatographed on alumina from trichlorobenzene. Development with chlorobenzene and then with toluene containing 1% of acetone gave two main bands. The upper orange-yellow zone on extraction with aqueous pyridine gave yellow needles (0·08 g.) of *2 : 2′-azoxyfluorenone*, m. p. 331—332° (Found: C, 78·7; H, 3·6; N, 7·2. $C_{26}H_{14}O_3N_2$ requires C, 77·6; H, 3·5; N, 7·0%). It dissolves in concentrated sulphuric acid with an orange-red colour. A similar product, m. p. 329—331° (Found: C, 78·0; H, 3·8; N, 6·8%), was obtained by the action of alkaline stannous chloride on 2-nitrofluorenone.

2 : 2′-Azofluorenone.—A solution of the above azoxy-derivative (0·4 g.) in hot pyridine (50 ml.) was added in 15 min. to a vigorously stirred solution of sodium hydroxide (6 g.) and sodium dithionite (3 g.) in water (60 ml.) at 80—90°. Stirring was continued for 15 min. longer, then the solution was cooled; it formed two layers. The reddish-brown pyridine layer was added to water (200 ml.), and the resulting *2 : 2′-azofluorenone* was collected, dried, and crystallised several times from pyridine to give yellow needles, m. p. 338—340° (Found: C, 81·0; H, 3·6; N, 7·1. $C_{26}H_{14}O_2N_2$ requires C, 80·8; H, 3·6; N, 7·3%). The mixed m. p. with 2 : 2′-azoxyfluorenone was 311—324°. The solution in concentrated sulphuric acid was deep blue, tinged red.

CLOTHWORKERS' RESEARCH LABORATORY,
UNIVERSITY OF LEEDS.

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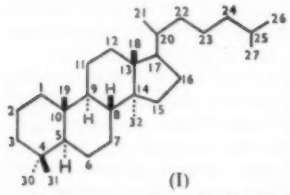
[11] Fletcher and Pan, *J. Amer. Chem. Soc.*, 1956, **78**, 4812.

239. *Infrared Spectra of Natural Products. Part VIII.* The Characterization of Carbonyl Groups and Ethylenic Double Bonds in Tetracyclic Triterpenoids.*

By A. R. H. Cole and R. L. S. Willix.

Absorption bands related to carbonyl and ethylenic double bonds in compounds based on lanosterol have been studied with emphasis on the patterns of infrared absorption due to conjugated ketone systems formed by oxidation of centres near the 8 : 9-double bond. These patterns, with their associated ultraviolet absorption, are useful in structural investigations, and additional structural information may be obtained from bands due to adjacent methylene groups. The regions of ethylenic C–H stretching and bending vibrations have also been studied for some of the compounds.

The tetracyclic triterpenoids [1] form a useful bridge in extending the well-known steroid infrared data [2] to the more complex pentacyclic triterpenoids.[1a,3,4] The absorption frequencies of functional groups would be expected to depend on position in the molecule as in the cholestane series. However, small but significant shifts might occur due to the altered mass relations caused by the additional methyl groups, and the absorption of these groups will alter the appearance of the spectra in the regions of C–H stretching and bending absorption.



(I)

The common triterpenoids differ from the common steroid derivatives notably in including compounds which contain complex conjugated ketone systems in rings B and C. The ultraviolet absorption due to these systems [5] is useful for identification and in the present work particular attention is paid to their characteristic infrared patterns.

The compounds studied here are nearly all based on lanostane (I) (a preliminary account of some of the results has been published [2c]). Most of the results will be readily applicable to similar triterpenoids based on eburicane and euphane.[5]

Experimental

To minimise the effects of intermolecular interaction,[6] all compounds were studied in dilute solution in carbon tetrachloride, chloroform (2·5—8 μ, calcium fluoride prism, single pass), or carbon disulphide (8—15 μ, sodium chloride prism, double pass). For the short-wavelength region carbon tetrachloride is preferred (and most of the ensuing discussion is based on measurements in this solvent), but representative compounds were studied in chloroform since many natural acids and polyhydroxy-compounds are insufficiently soluble in carbon tetrachloride. Carbonyl frequencies are between 3 and 20 cm.$^{-1}$ lower in chloroform,[2a] the corresponding solvent shift for ethylenic double-bond frequencies being 1—5 cm.$^{-1}$ and often not significant. The infrared spectrometer and general experimental conditions have been described.[4] Spectral slit widths were approximately 5 cm.$^{-1}$ at 3000 cm.$^{-1}$, 3 at 1700 cm.$^{-1}$ and 2 at 800 cm.$^{-1}$ and apparent molar extinction coefficients are accurate within about 5%.

Results and Discussion

The band frequencies for the individual compounds are listed in Tables 1—4 and characteristic frequencies for different structures are summarised in Tables 5 and 6. Apart

* Part VII, *J.*, 1957, 1332.

[1] (*a*) Jeger, *Fortschr. Chem. org. Naturstoffe*, 1950, **7**, 1; (*b*) Jones and Halsall, *ibid.*, 1955, **12**, 44; Gascoigne and Simes, *Quart. Rev.*, 1955, **9**, 328.

[2] (*a*) Jones and Herling, *J. Org. Chem.*, 1954, **19**, 1252; (*b*) Cole, *Rev. Pure Appl. Chem.* (*Australia*), 1954, **4**, 111; (*c*) Cole, *Fortschr. Chem. org. Naturstoffe*, 1956, **13**, 1.

[3] White, *Rev. Pure Appl. Chem.* (*Australia*), 1956, **6**, 191.

[4] Cole and Thornton, *J.*, 1956, 1007.

[5] For a summary, see Jones and Halsall, ref. 1.

[6] Cole, *Chem. and Ind.*, 1954, 661.

from carbonyl and C=C stretching frequencies, the Tables include representative measurements in the regions of ethylenic C–H stretching and bending vibrations and " adjacent methylene " vibrations,[7] all of which give valuable information in structural investigations. For example, in the non-conjugated ketones the frequency of the 3-carbonyl group (1708 cm.$^{-1}$) is hardly significantly higher than that of the 11-carbonyl group (1703—1706 cm.$^{-1}$), but with the high dispersion of a calcium fluoride prism near its long-wave cut-off there is no difficulty in distinguishing the adjacent methylene groups ($C_{(2)}$ at 1426—1427 cm.$^{-1}$, $C_{(12)}$ at 1432—1433 cm.$^{-1}$). It is interesting that the frequency of the 2-methylene group in the tetracyclic triterpenoid 3-ketones is intermediate between those found for the pentacyclic triterpenoid 3-ketones [4] (1429 cm.$^{-1}$) and the steroid 3-ketones [7] (1422 cm.$^{-1}$).

In the presence of a Δ^8-7-ketone grouping, the frequency of the 3-carbonyl group is raised to 1713—1715 cm.$^{-1}$. This must be due to extra strain in ring A because of the flattening of ring B by the conjugated system.

TABLE 1. *Frequencies (cm.$^{-1}$), with some peak intensities (in parentheses), of bands characteristic of non-conjugated carbonyl groups. In this and subsequent Tables, a blank space indicates that the region was not examined while a dash indicates that no band was found.*

C=O (CCl_4)	Compound	C=O ($CHCl_3$)	CH_2 adjacent to C=O (CCl_4)
	3-Ketones		
1708	Lanost-8-en-3-one	1700(490)	1427
1708(590)	9 : 19-*cyclo*Lanost-24-en-3-one (*cyclo*Artenone)	1697	
1713(550)	Lanost-8-ene-3 : 7-dione *	1705	1427
1715	Lanost-8-ene-3 : 7 : 11-trione *		1426
	11-Ketones		
1703(510)	3β-Acetoxylanostan-11-one *		1432
1704(500)	3β-Acetoxylanost-5-en-7 : 11-dione *	1703	1432
1706	3β-Hydroxylanost-5-en-7 : 11-dione *		1433
	7 : 11-Diketones		
1705	3β-Hydroxylanostane-7 : 11-dione		1432
1707(800)	Me 3β-acetoxy-7 : 11-dioxo-25 : 26 : 27-trisnorlanostan-24-oate *	1703	
1708(820)	3β-Acetoxylanostane-7 : 11-dione *	1703	1433
1712(1180) [a]	3β-Benzoyloxy-4 : 4 : 14-trimethyl-5α-pregnane-7 : 11 : 20-trione		1432, 1357
1712(1450) [c] / 1760(170) [d]	3β-Benzoyloxy-7 : 11-dioxo-25 : 26 : 27-trisnorlanostan-24-oic acid		1431
	3 : 7 : 11-Triketone		
1711(1040)	Lanostane-3 : 7 : 11-trione	1703	1430
	Five-membered ring ketones		
1741	A-Nor-30 : 31-bisnorlanost-8-en-3-one		1407(67)
1747 [e]	3β : 7β : 11α-Tribenzoyloxy-4 : 4 : 14-trimethyl-5α-androstan-17-one *		1411
	3β : 7β : 11α-Triacetoxy-4 : 4 : 14-trimethyl-5α-androstan-17-one		1412

* These compounds have one or more additional carbonyl bands, the frequencies of which are given in other sections.
[a] Includes C=O absorption of BzO and AcO groups. [b] Methyl bending frequency of COMe. [c] Includes C=O absorption of BzO group and dimeric acid. [d] Monomeric acid. [e] Sodium chloride prism.

For non-conjugated 7 : 11-diones and the 3 : 7 : 11-triones the individual carbonyl and adjacent methylene bands are not resolved, but the high carbonyl intensity indicates the presence of more than one group. Although the true measure of intensity is the integrated band area,[8] the peak heights given here may be useful as giving an idea of the expected

[7] Jones and Cole, *J. Amer. Chem. Soc.*, 1952, **74**, 5648; Jones, Cole, and Nolin, *ibid.*, pp. 5662, 6321.
[8] Ramsay, *J. Amer. Chem. Soc.*, 1952, **74**, 72; Jones, Ramsay, Keir, and Dobriner, *ibid.*, p. 80.

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TABLE 2. *Frequencies (cm.$^{-1}$), with some peak intensities (in parentheses), of bands characteristic of conjugated carbonyl groups.*‡

C=C (CCl_4)	C=O (CCl_4)	Compound	C=O ($CHCl_3$)	C=C ($CHCl_3$)	CH_2 adjacent to C=O (CCl_4)	CH_2 adjacent to C=C (CCl_4)	Ethylenic CH bend (CS_2)
		Δ^5-7-*Ketones*					
1609	1667	3β-Hydroxylanost-5-ene-7 : 11-dione *			1433		
1610(90)	1668(640)	3β-Acetoxylanost-5-ene-7 : 11-dione *	1663				803, 794
		Δ^8-7-*Ketones*					
†	1665	3β-Hydroxylanost-8-en-7-one			1417	1425	
†	1666(620)	3β-Acetoxylanost-8-en-7-one *	1653	1583	1420	1420	
†	1670(510)	Lanost-8-ene-3 : 7-dione *	1660	1585	1418	1427	
		Δ^8-11-*Ketone*					
†	1657(550)	3β-Acetoxylanost-8-en-11-one *	1646	1584	1418	1428	
		Δ^8-7 : 11-*Diketones*					
—	1676(770) 1685(sh)	3β-Acetoxylanost-8-ene-7 : 11-dione *	1673	—	1428		
—	1676 1690	Lanost-8-ene-3 : 7 : 11-trione *			1426		
—	1677 1685(sh)	3β-Hydroxylanost-8-ene-7 : 11-dione			1427		
—	1677(700) 1684(sh)	3β-Benzoyloxylanost-8-ene-7 : 11-dione *	1673	—	1428		
—	1677(790) 1685(sh)	Methyl 3β-benzoyloxy-7 : 11-dioxo-25 : 26 : 27-trisnorlanost-8-en-24-oate *	1673	—			
		$\Delta^{5:8}$-7 : 11-*Diketone*					
1623(110)	1673(510) 1654(905)	3β-Acetoxylanosta-5 : 8-diene-7 : 11-dione *	1668 1648	1620	1426		813
		$\Delta^{5:8}$-7 : 11 : 12-*Triketones*					
1620(100)	1737(315) 1685(590) 1650(960)	Lanosta-5 : 8-diene-7 : 11 : 12-trione	1736 1681 1646	1615	(ethylenic CH str 3075 cm.$^{-1}$)	—	820, 790, 768, 730
1619(100)	1738(320) 1686(560) 1655(980)	3β-Hydroxylanosta-5 : 8-diene-7 : 11 : 12-trione	1735 1682 1648	1618		—	820, 788, 769, (34) (64) (24) 731 (30)
1622(95)	1740(770)* 1684(570) 1656(940)	3β-Acetoxylanosta-5 : 8-diene-7 : 11 : 12-trione	1732 1682 1650	1620		—	820, 793, 769, 734
1631(130)	1737(315) 1685(500) 1656(940)	Lanosta-2 : 5 : 8-triene-7 : 11 : 12-trione	1733 1681 1646	1627	(ethylenic CH str 3075 cm.$^{-1}$)	1412 [b]	821, 795, 772, (30) (22) (33) 748,[b] 730 (80) (48)
		$\Delta^{5:8:11}$-7-*Ketone*					
1615(~400)	1647(900)	Lanosta-5 : 8 : 11-trien-7-one			(ethylenic CH str 3047, 3010 cm.$^{-1}$)		830, 749,[b] 729
		$\Delta^{3:5:8}$-7 : 11 : 12-*Triketone*(iso)					
1631(710)	1735(390) 1682(630) 1645(880)	3-*iso*Propylidene-A-nor-30 : 31-bisnorlanosta-5 : 8-diene-7 : 11 : 12-trione (*iso*lanostatrienetrione)					
		Δ^{24}-26-*Aldehyde*					
1650(85)	1692(750)	3β-Acetoxylanosta-8 : 24-dien-26-al *	1681	1645	1420	1434	817

* See footnote to Table 1. † Obscured by solvent absorption. ‡ A blank space indicates that the region was not investigated; a dash indicates that the region was investigated but no absorption band found. sh = unresolved shoulder.

[a] Includes C=O absorption of OAc group. [b] Attributed to the *cis*-disubstituted double bond.

TABLE 3. *Frequencies (cm.$^{-1}$), with some peak intensities (in parentheses), of bands characteristic of ethylenic double bonds.*[*]

	Ethylenic CH stretch (CCl_4)	C=C (CCl_4)	CH_2 adjacent to C=C (CCl_4)	Ethylenic CH bend (CS_2)
(A) Non-conjugated C=C.				
Δ^7-Compound				
Lanost-7-en-3β-yl acetate	3030	(1662)[a]	1435	822
Δ^8-Compounds				
Lanost-8-ene	—	—	1434	—
Lanost-8-en-3β-yl acetate	—	—	1434	—
3β-Acetoxylanosta-8 : 24-dien-26-al	—	—	1434	—
Lanost-8-en-3β-ol	—	—	1435	—
Lanost-8-en-3-one	—	—	1435	—
Lanosta-8 : 24-diene	—	—	1435	—
Lanosta-8 : 24-dien-3β-yl acetate	—	—	1435	—
A-Nor-30 : 31-bisnorlanost-8-en-3-one	—	—	1435	—
3-*iso*Propylidene-A-nor-30 : 31-bisnor-lanost-8-ene (*iso*lanostadiene)	—	—	1435	—
$\Delta^{9(11)}$-Compounds				
Lanost-9(11)-en-3β-ol	3053	—	1435	815
Lanost-9(11)-en-3β-yl acetate	3053	—	1435	815
Δ^{24}-Compounds				
Lanosta-8 : 24-diene		1673(15)		
Lanosta-8 : 24-dien-3β-yl acetate				829
9 : 19-*cyclo*Lanost-24-en-3-one		1673		836(35)
Δ^{25}-Compounds				
9 : 19-*cyclo*Eburic-25-en-3β-ol (*cyclo*-Laudenol)	3040,[b] 3071			887
9 : 19-*cyclo*Eburic-25-en-3β-yl acetate	3040,[b] 3071			887
9 : 19-*cyclo*Eburican-3β-yl acetate	3040,[b] —			—
(B) Conjugated C=C.				
$\Delta^{7:9(11)}$-Dienes				
Lanosta-7 : 9(11)-diene	3030(45)	1629	1432	814, 800
Lanosta-7 : 9(11)-dien-3β-ol	3032	1629	1432	814, 800
Lanosta-7 : 9(11)-dien-3β-yl acetate	3028		1432	814, 800
$\Delta^{8:7:9(11)}$-Triene (iso)				
3-*iso*Propylidene-A-nor-30 : 31-bisnor-lanosta-7 : 9(11)-diene (*y*-lanostatriene)	3015		1430	810

[*] A blank space indicates that the region was not investigated; a dash indicates that the region was investigated but no absorption found.

[a] Very weak band; frequency uncertain because of water-vapour absorption in background.

[b] *cyclo*Propyl ring absorption (ref. 11).

TABLE 4. *Miscellaneous ester carbonyl frequencies (cm.$^{-1}$) and benzoate* CH *frequencies.*

Compound	No. of compounds	C=O (CCl_4)	C=O ($CHCl_3$)	Aromatic CH stretch	Aromatic CH out-of-plane
Acetates	15	1733—1741	1720—1730		
Benzoates	4	1718—1720	1709—1713	3066—3071	711
Me esters	2	1740			

intensity, partly for identification and partly as an aid in deciding solution concentrations and cell lengths when recording spectra.

The five-membered ring ketones, obtained as oxidation products, have characteristic carbonyl frequencies near 1740 cm.$^{-1}$ which would not be confused with that of a normal six-membered ring carbonyl, but one of the bands of the $\Delta^{5:8}$-7 : 11 : 12-trione system (see below) lies as high as 1737—1740 cm.$^{-1}$. Also the acetate-carbonyl absorption (1733—1741 cm.$^{-1}$) usually obscures part or all of the five-membered carbonyl band and when looking for this type of group it is preferable to use benzoates (1718—1720 cm.$^{-1}$) if esterification of hydroxyl groups is necessary to increase solubility or to prevent hydrogen-bonding. In the presence of acetates, however, positive identification of the five-membered ring carbonyl can usually be obtained from the adjacent methylene absorption near 1407—1410 cm.$^{-1}$. Intensity measurements on this band have been used to determine the

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number of CH_2 groups adjacent to a five-membered ring-carbonyl group in compounds related to lanosterol [9] and phyllocladene.[10]

TABLE 5. *Average* C=O *and double-bond characteristic frequencies* (*cm.*$^{-1}$).

CCl_4 Soln.			$CHCl_3$ Soln.	
C=C	C=O	Compound	C=O	C=C
	1708	3-Ketone	1699	
	1714	Δ^5-3 : 7-Diketone	1705	
	1704	11-Ketone	1703	
	1709	7 : 11-Diketone	1703	
	1711	3 : 7 : 11-Triketone	1703	
	1741	A-Nor-3-ketone		
	1747	17-Ketone		
1610	1668	Δ^5-7-Ketone	1663	
	1667	Δ^8-7-Ketone	1657	1584
	1657	Δ^8-11-Ketone	1646	1584
—	1677, 1686	Δ^8-7 : 11-Diketone	1673	—
1623	1673, 1654	$\Delta^{5:8}$-7 : 11-Diketone	1668, 1648	1620
1620	1738, 1685, 1655	$\Delta^{5:8}$-7 : 11 : 12-Triketone	1734, 1682, 1648	1618
1615	1647	$\Delta^{5:8:11}$-7-Ketone		
1631	1735, 1682, 1645	$\Delta^{3:5:8}$-7 : 11 : 12-Triketone		
1650	1692	Δ^{24}-26-Aldehyde	1681	1645
1673		24 : 25-C=C		
1629		$\Delta^{7:9(11)}$-Diene		

TABLE 6. *Frequencies* (*cm.*$^{-1}$) *of methylene groups adjacent to* C=O *and* C=C *centres* (CCl_4 *solution*). *The position of the absorbing group is given in parentheses.*

	CH_2 adjacent to C=O	CH_2 adjacent to C=C
3-Ketone	1426—1427 (C_2)	
11-Ketone	1432—1433 (C_{12})	
7 : 11-Diketone	1431—1433 (C_6, C_{12})	
A-Nor-3-ketone	1407 (C_2)	
Δ^8-7-Ketone	1417—1420 (C_6)	1425—1427 (C_{11})
Δ^8-11-Ketone	1418 (C_{12})	1428 (C_7)
Δ^8-7 : 11-Diketone ...	1426—1428 (C_6, C_{12})	
$\Delta^{5:8}$-7 : 11-Diketone	1426 (C_{12})	

	CH_2 adjacent to C=C
Δ^{24}-26-Aldehyde	1420 (C_{23})
2 : 3-C=C	1412 (C_1)
7 : 8-C=C	1435 (C_6)
8 : 9-C=C	1434—1435 (C_7, C_{11})
9 : 11-C=C	1435 (C_{12})
$\Delta^{7:9(11)}$-Diene	1432 (C_6, C_{12})
$\Delta^{3:7:9(11)}$-Triene ((iso)	1430 (C_3, C_6, C_{12})

The carbonyl absorption of the carboxylic acid included in section 3 of Table 1 is considered in more detail in Part XII of this series (below).

The identification of isolated ethylenic centres (Table 3*A*) is not easy by single-beam infrared spectroscopy since their stretching absorption is very weak and is partly obscured by absorption by atmospheric water-vapour. Such a band was found with certainty only in the case of the Δ^{24}-compounds, but with the other types assistance in identification is obtained in other regions of the spectrum. The adjacent methylene band at **1435** cm.$^{-1}$ is particularly useful in telling the presence of the **8 : 9**-double bond which, being symmetrical, has no C=C stretching absorption and, since it is fully substituted, can give no ethylenic C–H stretching or bending absorption. Ring strain due to the neighbouring five-membered D-ring raises the ethylenic C–H stretching frequency of the $\Delta^{9(11)}$-compounds to **3053** cm.$^{-1}$, while in the *cyclo*laudenol derivatives bands due to both the vinylidene group (3071 cm.$^{-1}$) and the *cyclo*propane ring [11] (3040 cm.$^{-1}$) are well resolved.

For conjugated diones and ketones the frequencies of both the carbonyl and the ethylenic centre are lowered and their intensities increased with respect to the corresponding non-conjugated compounds. Some of the C=C bands (*e.g.*, for Δ^8-7- and Δ^8-11-ketones) fall at too low a frequency to be studied in carbon tetrachloride but can be easily found in

[9] Barnes, Barton, Cole, Fawcett, and Thomas, *J.*, 1953, 571.
[10] Bottomley, Cole, and White, *J.*, 1955, 2624.
[11] Cole, *J.*, 1954, 3807.

chloroform solution. The 8 : 9-ethylenic centre is no longer symmetrical in these conjugated ketones and its stretching absorption shows up clearly near 1584 cm.$^{-1}$ (in chloroform). *trans*-Fusion of the five-membered D-ring with the C-ring tends to flatten the latter, making the ethylenic bond and the 11-carbonyl group more nearly coplanar and facilitating conjugation. This is reflected in its carbonyl frequency (1657 cm.$^{-1}$), which is lower than that for the Δ^8-7-carbonyl group (1665—1670 cm.$^{-1}$), and this difference suffices to distinguish the two in oxidation products.

For these conjugated ketones the hyperconjugative effect on the adjacent methylene groups is enhanced, and usually two bands can be resolved, *viz.*, 1417—1420 cm.$^{-1}$ for the CH_2 next to the carbonyl and 1425—1428 cm.$^{-1}$ for that next to the ethylenic bond.

In the Δ^8-7 : 11-diones the two carbonyl groups act in opposition in conjugating with the double bond. Two resolved peaks (1676, 1690 cm.$^{-1}$) are found in the spectrum of lanost-8-ene-3 : 7 : 11-trione (apart from the 3-ketone absorption at 1715 cm.$^{-1}$), and the lower of these we assign to the 11-carbonyl group since this appears to conjugate more effectively (see above). A similar effect has been reported [4] for $\Delta^{13(18)}$-pentacyclic triterpenoid 12 : 19-diketones. The other compounds in this class have an unsymmetrical carbonyl band with its peak near 1677 cm.$^{-1}$ and an unresolved shoulder near 1685 cm.$^{-1}$. In chloroform the absorption (1673 cm.$^{-1}$) is slightly broader than in carbon tetrachloride, and for the compounds studied here the asymmetry was not observed. A carbonyl frequency of 1671 cm.$^{-1}$ has been reported [12] for this system, but the medium was not named.

The relatively high carbonyl frequencies of these compounds support the view that conjugation is incomplete, and further evidence is found in the higher adjacent methylene frequency (1426—1428 cm.$^{-1}$) compared with the singly conjugated 7- and 11-ketones (1417—1420 cm.$^{-1}$). The 8 : 9-ethylenic centre in these diones is again symmetrical, and no stretching absorption could be found.

As the conjugated system becomes longer the pattern of infrared absorption becomes more complex. 3β-Acetoxylanosta-5 : 8-diene-7 : 11-dione shows, apart from its acetate-carbonyl absorption (1741 cm.$^{-1}$), bands at 1673 cm.$^{-1}$ (singly conjugated 11-ketone) and 1654 cm.$^{-1}$ (doubly conjugated 7-ketone), and a relatively intense 5 : 6-double-bond band at 1623 cm.$^{-1}$. In this compound also the conjugation of the two carbonyl groups is somewhat mutually opposed and the 11-carbonyl frequency is not as low as that of the simple Δ^8-11-ketones.

The carbonyl pattern is even more characteristic in the case of the $\Delta^{5:8}$-7 : 11 : 12-triketones. The bands should properly be considered to belong to the system as a whole, but those at 1650—1655 and 1684—1686 cm.$^{-1}$ can be attributed to the $\Delta^{5:8}$-7-ketone and the Δ^8-11-ketone respectively, while the high-frequency absorption (1737—1740 cm.$^{-1}$) is due to the 12-carbonyl group. This kind of frequency increase has been noted previously for 11 : 12-dioxo-steroids [13] and appears to be due to the increase in ring strain since the 12-carbonyl group cannot be said to be conjugated in the usual sense. The C=C stretching band near 1620 cm.$^{-1}$ is quite intense. For lanosta-2 : 5 : 8-triene-7 : 11 : 12-trione the 2 : 3-double bond must absorb on the high-frequency side of the conjugated double-bond absorption since only one band (1631 cm.$^{-1}$) is found. The adjacent methylene peak at 1412 cm.$^{-1}$ must be attributed to the 1-methylene group since the conjugated system has none of these groups.

The spectrum of lanosta-5 : 8 : 11-trien-7-one is notable for the very low frequency (1647 cm.$^{-1}$) and high intensity of the triply conjugated carbonyl group and the intense band at 1615 cm.$^{-1}$ due to the double bonds.

*iso*Lanostatrienetrione has its two higher carbonyl frequencies at much the same frequencies as the $\Delta^{5:8}$-7 : 11 : 12-triketones, but the increased conjugation leads to a further lowering of the 7-ketone frequency. The extremely intense band at 1631 cm.$^{-1}$

[12] Warren and Watling, *J.*, 1958, 179.
[13] Jones and Dobriner, *Vitamins and Hormones*, 1949, **7**, 293.

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cannot be attributed to any particular ethylenic bond, but must belong to the system as a whole.

The authors are grateful to Professor D. H. R. Barton, F.R.S., Professor F. S. Spring, F.R.S., and Dr. J. F. McGhie, who supplied the compounds. The infrared spectrometer was purchased through a generous grant from the Nuffield Foundation, to whom one of the authors (A. R. H. C.) is also indebted for a Fellowship.

UNIVERSITY OF WESTERN AUSTRALIA,
NEDLANDS, W. AUSTRALIA.

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240. *Infrared Spectra of Natural Products. Part IX.* Frequencies and Intensities of Hydroxyl Absorption Bands in Triterpenoids and Similar Compounds.*

By A. R. H. COLE, (MISS) G. T. A. MÜLLER, and (in part) D. W. THORNTON and R. L. S. WILLIX.

Accurate measurements have been made of the hydroxyl stretching frequencies of a number of triterpenoid and similar alcohols in carbon tetrachloride solution. Characteristic frequencies are found for primary (3640—3641 cm.$^{-1}$), axial secondary (3635—3638 cm.$^{-1}$), equatorial secondary (3628—3630 cm.$^{-1}$ at $C_{(3)}$; 3623—3635 cm.$^{-1}$ at $C_{(11)}$), and tertiary (3613—3618 cm.$^{-1}$) hydroxyl groups; it is probable that axial (3617 cm.$^{-1}$) can be distinguished from equatorial tertiary groups (3613 cm.$^{-1}$). Values of the peak apparent molar extinction coefficient, the apparent half band width, and integrated band intensities are given for most of the compounds. The mean value of the integrated intensity is $0{\cdot}60 \times 10^4$ l. mole^{-1} cm.$^{-2}$, and intensities are additive for more than one group in the molecule. Applications of the characteristic frequencies to determinations of organic structure are described.

ALTHOUGH primary, secondary, and tertiary hydroxyl groups have been reported as giving rise to slightly different Raman frequencies,[1] Bellamy has suggested that they cannot be distinguished by means of their infrared absorption,[2] but the examples quoted by him (benzyl alcohol and phenols) are not really typical of primary, secondary, and tertiary alcohols. Jones and Sandorfy [3] similarly doubted whether small frequency differences in this region are suitable for characterising the type of hydroxyl group because of overlap of hydrogen-bonded OH absorption; but this difficulty can be eliminated by using dilute solutions in carbon tetrachloride. We have measured the hydroxyl frequencies and intensities of a number of triterpenoids with primary, secondary, or tertiary groups in axial and equatorial orientations. Results indicating a significant difference in stretching frequency between axial (3637—3639 cm.$^{-1}$) and equatorial (3629—3630 cm.$^{-1}$) 3-hydroxyl groups have been published.[4] In this paper, attention is directed to the differences in frequency between primary, secondary, and tertiary groups, and a few measurements on secondary hydroxyl groups at positions other than 3 are described. Some of these frequencies have been used in interpreting the spectra of *cyclo*hexane-1 : 2-diols.[5]

EXPERIMENTAL

The spectrometer and general experimental conditions have been described.[6] The compounds were studied in carbon tetrachloride solutions at concentrations (<0·005M) too low to

* Part VIII, preceding paper.

[1] Bateuv and Matveeva, *Izvest. Akad. Nauk S.S.S.R., Otdel. Chim. Nauk,* 1951, 448.
[2] Bellamy, "The Infra-red Spectra of Complex Molecules," Methuen, London, 1954, p. 86.
[3] Jones and Sandorfy in "Technique of Organic Chemistry" (Ed. Weissberger), Interscience, New York, 1956, Vol. IX, p. 419.
[4] Allsop, Cole, White, and Willix, *J.*, 1956, 4868.
[5] Cole and Jefferies, *J.*, 1956, 4391.
[6] (*a*) Cole and Thornton, *J.*, 1956, 1007; (*b*) Cole and Willix, preceding paper.

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allow intermolecular hydrogen-bonding. A background spectrum of absorption by atmospheric water-vapour was recorded through a cell full of solvent on all charts immediately before that of the sample, and the sample spectrum was measured by subtraction of the background at a large number of points. The spectra were run slowly and the spectral slit width at 3630 cm.$^{-1}$ is estimated from the width of the lines in the water-vapour spectrum to be 6 cm.$^{-1}$. In this way peak frequencies can be measured to ± 1 cm.$^{-1}$ and intensities to about $\pm 5\%$.

Results and Discussion

The hydroxyl frequencies and peak apparent molar extinction coefficients [7] [$\varepsilon = (1/cl) \log_{10} (T_0/T)$] for the individual compounds are given in Table 1 and are summarised

Table 1. *Hydroxyl stretching frequencies (cm.$^{-1}$ in CCl_4) and intensity data.*

	ν (cm.$^{-1}$)	$\varepsilon_{max.}$	$\Delta\nu_{\frac{1}{2}}$ [a]	$10^{-4}A$
Primary				
Lup-20(29)-en-28-ol	3641	66	24	0·57
3β-Acetoxyolean-18-en-28-ol	3641	60	25	0·54
3β-Acetoxylup-20(29)-en-28-ol	3640	—	—	—
Primary + secondary (equatorial)				
Lup-20(29)-ene-3β : 28-diol (betulin)	3637	110	34	1·33
Lupane-3β : 28-diol	3636	—	—	—
Urs-12-ene-3β : 28-diol (uvaol) [a]	3625	107	—	—
Secondary. (i) *Equatorial* [b]				
Olean-18-en-3β-ol (morol)	3629	50	32	0·57
28-Norolean-17-en-3β-ol (oleanol)	3629	53	30	0·57
3β-Hydroxyoleanan-12-one	3628	65	28	0·65
Me 3β-hydroxyolean-12-en-28-oate (oleanolate)	3629	61	32	0·69
Me 3β-hydroxy-12-oxo-oleanan-28-oate	3628	57	—	—
Me 3β-hydroxyurs-12-en-28-oate (ursolate)	3630	54	32	0·61
13 : 27-*cyclo*Ursan-3β-ol (phyllanthol)	3629	59	32	0·67
Lupan-3β-ol	3628	62	27	0·60
Lup-20(29)-en-3β-ol (lupeol)	3629	55	30	0·58
Lanost-8-en-3β-ol	3629	60	30	0·65
Lanost-9(11)-en-3β-ol	3629	64	25	0·57
Lanosta-7 : 9(11)-dien-3β-ol	3629	58	31	0·64
3β-Hydroxylanost-8-en-7-one	3629	55	—	—
3β-Hydroxylanostane-7 : 11-dione	3629	50	34	0·61
3β-Hydroxylanost-8-ene-7 : 11-dione	3629	60	27	0·58
3β-Hydroxylanost-5-ene-7 : 11-dione	3629	60	28	0·60
9 : 19-*cyclo*Eburic-25-en-3β-ol (*cyclo*laudendol)	3629	58	33	0·68
Friedelan-3α-ol (friedelinol)	3630	—	—	—
3β-Acetoxylanostan-11α-ol	3623	50	—	—
7β-Acetoxylanostan-11α-ol	3625	—	—	—
3β : 7β-Diacetoxylanostan-11α-ol	3625	55	—	—
(ii) *Axial* [b]				
Me 3β-acetoxy-19α-hydroxy-12-oxo-oleanan-28-oate	3638	64	—	—
3β : 28-Diacetoxyolean-12-en-19α-ol	3641	—	—	—
Friedelan-3β-ol (*epi*friedelinol)	3635	—	—	—
3β-Acetoxy-12α : 13β-dihydroxyoleanan-28-oic 13-lactone	3624 [c]	—	—	—
(iii) *Equatorial + axial*				
Me 3β : 19α-dihydroxy-12-oxo-oleanan-28-oate	3633	90	33	1·00 [d]
Me 3β : 19α-dihydroxyolean-12-en-28-oate (siaresinolate)	3632	95	35	1·20 [d]
Tertiary. (i) *Equatorial*				
3α-Methylcholestan-3β-ol	3613	73	20	0·52
(ii) *Axial*				
3β-Methylcholestan-3α-ol	3617	70	20	0·50
p-Methan-4-ol	3619	—	—	—
(iii) *Miscellaneous* [e]				
Guaiol	3618	—	—	—

[a] $CHCl_3$ solution. [b] See also Allsop *et al.*[4] and Cole and Michell.[11] [c] See text. [d] Intensity measured by graphical integration to 70 cm.$^{-1}$ on either side of maximum + 15% wing correction. [e] See also Jones *et al.*[9]

[7] Ramsay, *J. Amer. Chem. Soc.*, 1952, **74**, 72.

TABLE 2. *Characteristic hydroxyl frequencies (cm.$^{-1}$) (CCl_4 solution).*

Primary	3640—3641	Secondary equatorial	$C_{(3)}$ 3628—3630	Tertiary axial	3617—3619
Secondary axial	3635—3638		$C_{(11)}$ 3623—3625	Tertiary equatorial	3613

in Table 2. In a few cases samples were too small or solubility too low for quantitative measurements. Primary (3640—3641 cm.$^{-1}$) and secondary equatorial (3628—3630 cm.$^{-1}$) groups, the two most common types, can easily be identified by their stretching frequencies. Further, as already pointed out,[4] secondary equatorial groups can be readily distinguished from axial (3637—3639 cm.$^{-1}$), although the latter cannot be differentiated with certainty from primary groups by this means. However, observations at lower frequency [8] might help in the absence of interfering groups (*e.g.*, esters) with strong absorption bands, and oxidation to the corresponding ketone (C=O frequency ~1700—1712 cm.$^{-1}$) or aldehyde (~1730 cm.$^{-1}$) will certainly resolve the pair.

The axial 19-hydroxyl group in the siaresinolic acid derivatives has the same high frequency (~3638 cm.$^{-1}$) as that at position 3, while an equatorial 7-hydroxyl group absorbs just below (~3625 cm.$^{-1}$) its equivalent at position 3. Friedelan-3α- and -3β-ol are consistent with other secondary types with the axial hydroxyl band 5 cm.$^{-1}$ higher than the equatorial.

Tertiary hydroxyl groups do not occur often in triterpenoids, but the spectra of a few similar compounds (Table 1) show that this type of group absorbs near 3618 cm.$^{-1}$ in carbon tetrachloride,[5,9] and this is easily distinguished from the others. The two methyl cholestanols and *p*-menthan-4-ol show a small difference, in the same sense as for secondary groups, between equatorial and axial hydroxyl groups and, although the number of examples is small, we believe this difference to be significant.

The low hydroxyl frequency (3624 cm.$^{-1}$) of the axial 12α-group in 3β-acetoxy-12α : 13β-dihydroxyoleanan-28-oic 13-lactone is undoubtedly due to the presence of the neighbouring lactone ring. An interaction between the two groups has been reported [6a] in dealing with triterpenoid carbonyl frequencies.

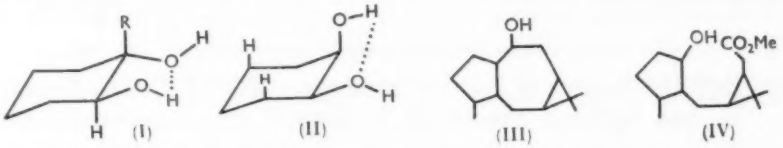
Compounds with more than one type of hydroxyl group absorb at an intermediate frequency [primary + secondary(*eq*) 3636—3637 cm.$^{-1}$; secondary(*eq*) + secondary(*ax*) (3632—3633 cm.$^{-1}$], since the band width (~25 cm.$^{-1}$) is too great for them to be resolved. However, intensity measurements can be used to determine the number of groups present (see below). In practice, low solubility of compounds containing more than two hydroxyl groups will prevent measurements in carbon tetrachloride, but chloroform * may be suitable for triols and tetrols. Hydroxyl frequencies are lower by about 10 cm.$^{-1}$ in chloroform (see uvaol, Table 1, and ref. 11).

Origin of the frequency differences between (a) *primary, secondary, and tertiary groups and* (b) *equatorial and axial groups.* (*a*) The decreasing order of stretching frequencies from primary to tertiary hydroxyl groups can be attributed to a reduction of the bond polarity $-\bar{O}-\overset{+}{H}$ due to the electron-releasing tendency of the C–H bonds of the primary and secondary groups. This is reflected in the known order of increasing acidity of alcohols, *viz.*, primary, secondary, tertiary. The greater electron-density on the oxygen of a tertiary group also gives an explanation for the observation by Cole and Jefferies [5] that in *cyclo*hexane-*trans*-1 : 2-diols, where both hydroxyl groups are equatorial, a secondary hydroxyl group tends to form a hydrogen bond to the oxygen of a tertiary group (cf. I), rather than the reverse.

* Chloroform, as usually supplied, contains about 0·5% of ethanol as stabiliser and this must be removed.[10]

[8] For summary, see ref. 3, p. 433.
[9] Jones, Humphries, Herling, and Dobriner, *J. Amer. Chem. Soc.*, 1952, **74**, 2820.
[10] Cole, *Fortschr. Chem. org. Naturstoffe*, 1956, **13**, 17.
[11] Cole and Michell, Part XII of this series, below.

(*b*) The higher stretching frequency of an axial than of an equatorial group appears to be due to steric factors rather than bond polarities. Repulsion of axial hydrogen atoms or other substituent groups would cause an axial hydroxyl group to be oriented about the C–O bond so that its hydrogen would lie on the side remote from the other axial atoms or groups, while an equatorial hydroxyl group is free to assume practically any orientation



about its C–O bond. Since the oxygen bond-angle is only slightly greater than 90°, the motion of the oxygen atom in the O–H stretching vibration is approximately at right angles to the C–O bond, and in an axial alcohol this is opposed by the repulsion of neighbouring axial groups. This repulsion could easily account for the small increase in force constant and the higher axial frequency (see also the following paper). This hypothesis is supported by the second observation by Cole and Jefferies [5] that in *cyclo*hexane-*cis*-1 : 2-diols, where one hydroxyl group is equatorial and the other axial, the hydrogen of the axial group is bound to the equatorial oxygen atom regardless of whether the groups are secondary or tertiary: this is the only direction in which hydrogen-bonding is possible if the hydroxyl-hydrogen is oriented away from the neighbouring axial hydrogen atoms (cf. II).

Hydroxyl intensities. Peak values of the apparent molar extinction coefficient are given for most of the compounds in Table 1, together with apparent half band widths ($\Delta\nu_{\frac{1}{2}}^{a}$). The integrated band intensities [$A = 2{\cdot}303 \times 1{\cdot}55\varepsilon_{max}\Delta\nu_{\frac{1}{2}}^{a}$ l. mole^{-1} cm.$^{-2}$] have been calculated by Ramsay's method I.[7] The hydroxyl bands are relatively broad compared with others (*e.g.*, for C=O [13] $\Delta\nu_{\frac{1}{2}}^{a} = 9$—14 cm.$^{-1}$; for CH_3 bending,[14] 6 cm.$^{-1}$), but they have a shape closely approximating to that of the Lorentz curve. The mean value of the hydroxyl integrated intensity ($0{\cdot}60 \times 10^4$ l. mole^{-1} cm.$^{-2}$) agrees fairly well with results for simple alcohols,[12] and the additivity of the intensities of individual groups is indicated by the results for betulin, methyl siaresinolate, and methyl 3β : 19α-dihydroxy-12-oxo-oleanan-28-oate. There appears to be little difference in intensity between primary, secondary, and tertiary groups. Measurements of peak height will often be sufficient to tell the number of hydroxyl groups in a new compound or degradation product, especially if they are of similar type and absorb at the same frequency. When they are of different kinds, particularly if primary and tertiary, the peak heights will not be additive because of the different positions of the individual bands, and integrated intensities should then be measured.

Applications. The foregoing results have been applied in a number of structural and degradative problems in this laboratory. Phillyrigenin [15] forms two monoacetates with hydroxyl bands (in $CHCl_3$) at 3614 (secondary) and 3625 cm.$^{-1}$ (primary) respectively. Methyl melaleucate [16] (in CCl_4) absorbs at 3629 cm.$^{-1}$ (equatorial secondary), while its 3-epimer obtained by oxidation to the ketone and reduction (Meerwein–Ponndorf) absorbs at 3636 cm.$^{-1}$ (axial secondary). Globulol [17] has a tertiary hydroxyl group (3615 cm.$^{-1}$, in CCl_4), and *apo*aromadendrol (III) (3629 cm.$^{-1}$, in CCl_4) and its degradation product (IV) (3628 cm.$^{-1}$, in CCl_4) both have secondary groups.

[12] Barrow, *J. Phys. Chem.*, 1955, **59**, 1129; Brown, Sandri, and Hart, *ibid.*, 1957, **61**, 698; Finch and Lippincott, *ibid.*, p. 894; Brown and Rogers, *J. Amer. Chem. Soc.*, 1957, **79**, 577.
[13] Jones, Ramsay, Keir, and Dobriner, *J. Amer. Chem. Soc.*, 1952, **74**, 80.
[14] Cole and Macritchie, unpublished results.
[15] Beckwith, Cole, Watkins, and White, *Austral. J. Chem.*, 1956, **9**, 428.
[16] Arthur, Cole, Thieberg, and White, *Chem. and Ind.*, 1956, 926.
[17] Blumann, Cole, Thieberg, and White, *ibid.*, 1954, 1426; Thieberg, Thesis, W. Australia, 1956; Jefferies, Melrose, and White, unpublished results.

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UNIVERSITY OF WESTERN AUSTRALIA,
NEDLANDS, WESTERN AUSTRALIA. [*Received, August 25th*, 1958.]

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241. *Infrared Spectra of Natural Products. Part X.* Conformations and Infrared Spectra of Substituted* cyclo*Hexanols.*

By A. R. H. COLE, P. R. JEFFERIES, and (MISS) G. T. A. MÜLLER.

Small but significant differences in the stretching frequencies of axial (3627—3632 cm.$^{-1}$) and equatorial (3622·5—3623 cm.$^{-1}$) hydroxyl groups are reported for a series of methyl*cyclo*hexanols and are used to determine the stable conformation of the compounds. The methyl group has a greater tendency to be equatorial than the hydroxyl, in agreement with kinetic studies. A similar difference in methyl bending frequency is reported (axial 1381, equatorial 1376—1377 cm.$^{-1}$) and this together with the difference in hydroxyl stretching frequency is attributed to steric interference by axial hydrogen atoms. Integrated intensities of the hydroxyl absorption band have been determined (mean value $0{\cdot}50 \times 10^4$ l. mole^{-1} cm.$^{-2}$) for nine compounds.

ALREADY [1-3] we have shown that axial and equatorial hydroxyl groups on *cyclo*hexane rings exhibit small, but characteristic, differences in stretching frequency with the axial frequency always slightly higher, and that primary, secondary, and tertiary groups can be identified by their stretching frequencies. In the present paper we report work on substituted *cyclo*hexanols in relation to hydroxyl absorption and stable conformations. The compounds include *cis*- and *trans*-2-, -3-, and -4-methyl*cyclo*hexanol, *cis*- and *trans*-4-*iso*propyl*cyclo*hexanol, and three methyl*cyclo*hexylmethanols. The experimental conditions were essentially the same as in the preceding paper.

The hydroxyl frequencies and intensities * are given in the Table. There is no doubt [2] that *trans*-dihydrocryptol exists in the diequatorial conformation (I; $R^1 = OH$, $R^2 = H$) and its *cis*-isomer as (I; $R^1 = H$, $R^2 = OH$), and the hydroxyl stretching frequencies of these [3623 (equatorial) and 3627 cm.$^{-1}$ (axial)] form a basis for determining the predominant conformation in the methyl*cyclo*hexanols. Both frequencies are lower than for the triterpenoids,[1,3] and this is probably related to the greater rigidity of the ring system in the more complex compounds. The menthols, with an extra substituent, and hence more inertia, give intermediate values. We previously [2] used an argument based on the tendency of *cyclo*hexanediols to form intramolecular hydrogen bonds to deduce that *neoiso*menthol exists predominantly as (II; $R^1 = R^3 = H$, $R^2 = Me$, $R^4 = OH$) and at that time did not fully realize the significance of slight differences in hydroxyl frequencies. Menthol (3628 cm.$^{-1}$) would be expected to have all groups equatorial (II; $R^1 = Me$, $R^2 = R^4 = H$, $R^3 = OH$) and it is immediately apparent from the Table that *iso*menthol exists in the conformation (II; $R^1 = R^4 = H$, $R^2 = Me$, $R^3 = OH$) in which the hydroxyl group is also equatorial (3627 cm.$^{-1}$), while both *neo*menthol and *neoiso*menthol (3632 cm.$^{-1}$) adopt the conformation in which it is axial. There is no doubt, then, that the relatively large *iso*propyl group acts as an equatorial anchor.

* See Part IX, preceding paper, for details. Some of the compounds were too volatile for quantitative measurements of intensity.

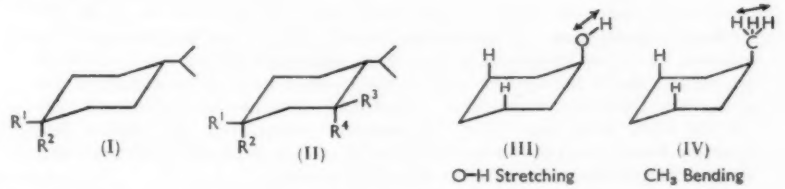
[1] Part IX, Cole, Müller, Thornton, and Willix, preceding paper.
[2] Cole and Jefferies, *J.*, 1956, 4391.
[3] Allsop, Cole, White, and Willix, *J.*, 1956, 4868.

Clearly, *cis*-2-methyl-, *trans*-3-methyl-, and *cis*-4-methyl-*cyclo*hexanol exist predominantly in the forms with axial hydroxyl groups (3627—3632 cm.$^{-1}$) while their isomers have equatorial hydroxyl groups (3622·5—3623 cm.$^{-1}$). For the diequatorial compounds this is to be expected, but for the others these results give a direct experimental proof of the tendency of the methyl group to adopt the equatorial configuration at the expense of the hydroxyl group, in agreement with Eliel and Lukach's results [4] based on a study of rates of

Hydroxyl frequencies (cm.$^{-1}$) and intensities (in carbon tetrachloride)

	ν (cm.$^{-1}$)	$\varepsilon_{max.}$	$\Delta\nu_{\frac{1}{2}}$[a]	$10^{-4}A$	Stable conformn. of OH group
cis-2-Methyl*cyclo*hexanol	3632	50	27	0·48	Axial
trans- ,, ,,	3622·5	—	—	—	Equatl.
cis-3-Methyl*cyclo*hexanol	3622·5	60	21·5	0·46	Equatl.
trans- ,, ,,	3627	60	19	0·41	Axial
cis-4-Methyl*cyclo*hexanol	3628	—	—	—	Axial
trans- ,, ,,	3623	60	21	0·45	Equatl.
cis-4-*iso*Propyl*cyclo*hexanol (*cis*-dihydrocryptol)	3627	65	21	0·49	Axial
trans- ,, ,,	3623	65	22	0·51	Equatl.
Menthol	3628	—	—	—	Equatl.
*iso*Menthol	3627	—	—	—	Equatl.
*neo*Menthol	3632	—	—	—	Axial
*neoiso*Menthol	3632	—	—	—	Axial
cis-2-Methyl*cyclo*hexylmethanol	3640	60	24	0·51	(Primary)
trans- ,, ,,	3641	65	25	0·58	(Primary)
cis-3-Methyl*cyclo*hexylmethanol	3641	65	25	0·58	(Primary)
trans-*p*-Menthan-4-ol	3619	—	—	—	Axial (tert.)

esterification of *cyclo*hexanols. The broad band width compared with the small frequency difference between equatorial and axial hydroxyl groups prevents the detection of small amounts of the less stable conformation, so that infrared measurements in this region do not provide enough results for calculation of equilibrium constants for the conformational transformation.



The results for the hydroxymethyl derivatives lend further support to the view [1] that primary hydroxyl groups can be readily identified by their high stretching frequency (3640—3641 cm.$^{-1}$ in CCl_4). It would be expected that the primary hydroxyl group, being the larger, would force the methyl group into the axial position in the *cis*-2-methyl compound while in the others both groups would be equatorial. We have confirmed this by examining the methyl bending region of the spectrum. The symmetrical bending frequencies of the equatorial methyl groups of *trans*-2- and *cis*-3-methyl*cyclo*hexylmethanol are at 1377 and 1376 cm.$^{-1}$ respectively, in agreement with methyl*cyclo*hexane [5] (1376 cm.$^{-1}$), while the corresponding frequency for the *cis*-2-methyl compound is higher (1381 cm.$^{-1}$). The steric repulsion of axial hydrogen atoms has been suggested [1] as the cause of the higher frequency of the OH stretching frequency (III) in axial secondary alcohols compared with equatorial, and if this is true the steric interference would be expected to raise the bending frequency (IV) of an axial methyl group relative to an equatorial. The unsymmetrical bending absorption of the methyl group is often obscured by ring-methylene

[4] Eliel and Lukach, *J. Amer. Chem. Soc.*, 1957, **79**, 598.
[5] Jones and Cole, *ibid.*, 1952, **74**, 5648.

bending absorption near 1450—1460 cm.$^{-1}$ but in these alcohols there is a significant shift of a band from 1456 cm.$^{-1}$ in the case of the two equatorial methyl groups to 1467 cm.$^{-1}$ for the *cis*-2-methyl (axial) compound, while the ring-methylene absorption remains at 1446—1447 cm.$^{-1}$. This higher axial bending frequency also supports the hypothesis above.

The frequency (3619 cm.$^{-1}$) of the tertiary hydroxyl group of *p*-methan-4-ol has been considered in the preceding paper. There can be no doubt that this group is axial since both the *iso*propyl and the methyl group oppose it for the equatorial orientation.

Hydroxyl Intensities.—The integrated intensities (Table) are slightly lower than those measured for triterpenoids,[1] but are in good agreement with results for simpler alcohols.[6] The measurements do not indicate any significant intensity difference between axial and equatorial groups.

The authors thank Professor John Read, F.R.S., Dr. A. Blumann, and Mr. G. J. H. Melrose who supplied some of the compounds. The infrared spectrometer was purchased through a generous grant from the Nuffield Foundation. A C.S.I.R.O. Senior Research Studentship (G. T. A. M.) and a Research Grant from the University of Western Australia are gratefully acknowledged.

UNIVERSITY OF WESTERN AUSTRALIA,
NEDLANDS, WESTERN AUSTRALIA. [*Received, August 25th,* 1958.]

[6] See preceding paper, ref. 12.

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242. *Infrared Spectra of Natural Products. Part XI.* Intramolecular Hydrogen-bonding and Stereochemistry of Triterpenoid Diols and Related Compounds.*

By A. R. H. COLE and (MISS) G. T. A. MÜLLER.

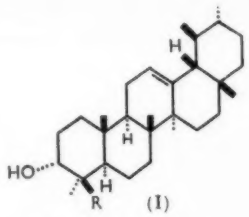
The presence or absence of intramolecular hydrogen-bonds in compounds based on *cyclo*hexane rings can be readily determined from the hydroxyl stretching absorption. Neighbouring diaxial groups are too far apart to interact, while two equatorial groups or an equatorial and an axial will form an intramolecular bond of varying strength depending on the nature of the groups and their stereochemistry. Spectra are described for a series of 3 : 23-(or 24)-diols, 3-hydroxy-23(or 24)-carbonyl compounds and 23(or 24)-hydroxy-3-ketones of the triterpenoid series, and the application of the results to new compounds or degradative work is described.

INFRARED absorption due to intramolecular hydrogen-bonding gives useful information about the stereochemistry of hydroxy-compounds [1-4] and few types of compound are as interesting for the investigation of this effect as those based on *cyclo*hexane rings with their axial and equatorial substituents. The present work is concerned with the stereochemistry of 3- and 4-substituents in triterpenoids. In a study of the infrared absorption of triterpenoid carboxylic acids [5] it was found that the spectrum of β-boswellic acid (I; R = CO_2H) in dilute solution in carbon tetrachloride showed no absorption due to intramolecular hydrogen-bonding, and that the high frequency of the 3-hydroxyl group (3638 cm.$^{-1}$) showed it to be axial.[6] This fixes the stereochemistry of ring A as (II; R = H), in agreement with the chemical evidence of Beton, Halsall, and Jones,[7] since only in the diaxial

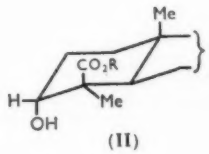
* Part X, preceding paper.

[1] Jones, Humphries, Herling, and Dobriner, *J. Amer. Chem. Soc.*, 1952, **74**, 2820, 6319.
[2] Kuhn, *ibid.*, p. 2492; 1954, **76**, 4323.
[3] Cole and Jefferies, *J.*, 1956, 4391.
[4] Henbest and Lovell, *J.*, 1957, 1965.
[5] (*a*) Michell, Thesis, W. Australia 1956; (*b*) Cole and Michell, in the press.
[6] Allsop, Cole, White, and Willix, *J.*, 1956, 4868.
[7] Beton, Halsall, and Jones, *J.*, 1956, 2904.

configuration are the hydroxyl and the carbonyl group sufficiently far apart to prevent hydrogen-bonding.



(I)



(II)

This work has now been extended to cover most of the known types of structure which might allow intramolecular hydrogen-bonding in this region.

Experimental.—The experimental conditions were as in Parts V and VIII.[8] All compounds were studied in dilute solution (<0·0035M) in carbon tetrachloride in a cell 10·0 mm. in length. Preliminary measurements at different concentrations showed the hydrogen-bonding to be intramolecular since the relative intensities of the bands due to free and bonded hydroxyl groups were independent of concentration.

Results and Discussion.—The relevant absorption frequencies with peak apparent molar extinction coefficients [$\varepsilon = (1/cl) \log_{10} (T_0/T)$] [9] are given in the Table. Apart from determining whether hydrogen-bonding exists, it is possible to state which of the hydroxyl groups in the dihydroxy-compounds is the donor and which the acceptor in the bonded system by examining closely the stretching frequency of the free hydroxyl group. In this type of compound, primary hydroxyl groups absorb at 3640—3642, axial secondary at 3637—3639, and equatorial secondary at 3628—3631 cm.$^{-1}$.[6,10]

(a) 3 : 24- and 3 : 23-*Dihydroxy-triterpenoids.* Urs-12-ene-3α : 24-diol (III) has the diaxial structure with no hydrogen bonding, while the spectrum of its 3β-isomer (IV)

Hydroxyl and carbonyl absorption frequencies (cm.$^{-1}$, CCl_4 solutions), with peak apparent molar extinction coefficients in parentheses.

Compound	Free OH	Bonded OH	Free C–O	Bonded C–O
Urs-12-ene-3α : 24-diol (III)	3641 (125)	—		
Urs-12-ene-3β : 24-diol (IV)	3629 (55)	3550 [a] (45)		
Me hederagenin (V)	3643 (100) 3628 (sh)	3532 [a] (70)	1729 [b] (450)	
Me 3α-hydroxyurs-12-en-24-oate (II; R = Me)	3638 (70)	—	1723 (580)	
Me 3β-hydroxyurs-12-en-24-oate (VIIA–B)	3627 [c]	3548 [a] (75)	1736 (70)	1709 (530)
Me gypsogenin (VIIIA–B)	3623 (50)	3549 [a] (40)	1729 [d] (575)	1710 (200)
β-Boswellic acid (II; R = H)	3638 (70) 3524 [a]	—	1737 (165)	1694 [f] (455)
Me hederagonate	3630 [c] 3602 (40)	3540 [a] (20)	1728 [b] (460)	1697 (340)
Me icterogenin	3635 (25)	3518 (35)	1746 [g] (450) 1718 [g,h] (435)	1694 (310)
Cerin	3615	3491 3436 [a]	1715	1709

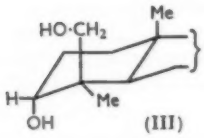
[a] Very broad. [b] Methoxycarbonyl. [c] Very weak. [d] Methoxycarbonyl plus non-bonded aldehyde. [e] Carboxyl-hydroxyl. [f] Dimeric acid (see ref. 5*b*). [g] Angelate carbonyl (see ref. 11). [h] Methoxycarbonyl plus non-bonded 3-ketone.

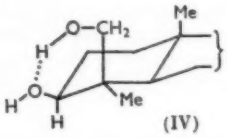
indicates that the primary hydroxyl is bonded to the oxygen of the equatorial secondary group (free OH, 3629 cm.$^{-1}$). This direction of bonding is probably due to the preferred orientation of the axial primary group away from the axial 10-methyl group.

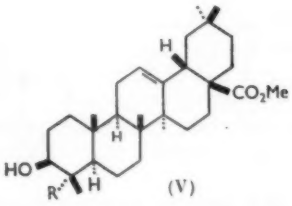
[8] (*a*) Cole and Thornton, *J.*, 1956, 1007; (*b*) Cole and Willix, *J.*, 1959, 1212.
[9] Ramsay, *J. Amer. Chem. Soc.*, 1952, **74**, 72.
[10] Cole, Müller, Thornton, and Willix, *J.*, 1959, 1218.

XUM

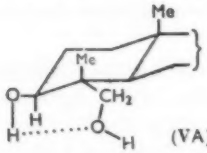
Methyl hederagenin (V; R = CH_2·OH), a 3β : 23-diol, exists mostly as (VA) (free primary OH 3643 cm.$^{-1}$) with a small proportion of (VB) [free secondary OH, 3628 cm.$^{-1}$ (shoulder)]. The methoxycarbonyl group absorbs at its normal position [8a] (1729 cm.$^{-1}$, see below).

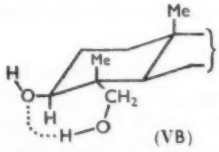

(III)

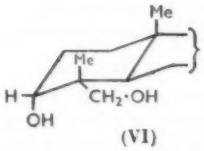

(IV)


(V)

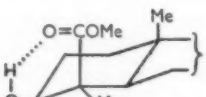
No sample of the second type of 3 : 23-diol (VI) was available. This structure would show hydrogen-bonding, probably as an equilibrium mixture as in (VA, VB), since the O–O distance in (VI) is the same as in (V) and the hydroxyl groups are not subject to steric repulsion by the 10-methyl group as in (IV).

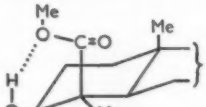

(VA)


(VB)


(VI)

(b) *Carbonyl compounds.* This method of studying stereochemistry can be extended to cover 3-hydroxy-23 (or 24)-ketones and 23 (or 24)-hydroxy-3-ketones. Hydrogen-bonding lowers the frequency of both the hydroxyl and the carbonyl group. Thus, while methyl 3α-hydroxyurs-12-en-24-oate (β-boswellate) (I; R = CO_2Me) has no hydrogen-bonding (II; R = Me) and shows normal hydroxyl (axial, 3635 cm.$^{-1}$) and carbonyl absorption (1723 cm.$^{-1}$), its 3β-epimer exists almost completely in the hydrogen-bonded form (VII) (C = O 1709 cm.$^{-1}$). The frequency of the weak residual carbonyl band (1736 cm.$^{-1}$) is rather high compared with that of the 3α-compound and might indicate the presence of a small amount of material in which the hydrogen-bond is formed on to the other oxygen atom [4] (VIIA). The presence of a very small proportion of non-bonded material (VIIB) is shown by the weak shoulder at 3627 cm.$^{-1}$.


(VII)


(VIIA)

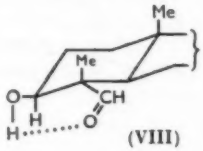
(VIIB)

The spectrum of methyl gypsogenin (V; R = CHO) indicates that the carbonyl group of an aldehyde is very much less effective as acceptor for a hydrogen-bond (VIII) than that of the methoxycarbonyl group, in agreement with the well-known electron-releasing properties of the methoxyl group. The high intensity of the free OH absorption band of this substance and the form of the carbonyl absorption show that in most of the molecules the hydroxyl group is free (VIIIA), although its frequency (3623 cm.$^{-1}$) is rather lower than usual for a secondary equatorial type. The carbonyl absorption consists of a major peak at 1729 cm.$^{-1}$ (methoxycarbonyl plus non-bonded aldehyde) with a shoulder at 1710 cm.$^{-1}$ due to the bonded carbonyl group.

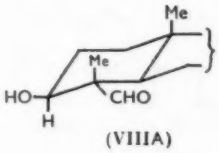
Methyl icterogenin [11] (IX) and methyl hederagonate (X) have respectively an axial and an equatorial primary 4-hydroxyl group which might be expected to form a hydrogen-bond

[11] Barton and de Mayo, *J.*, 1954, 887.

on to the 3-carbonyl group. The spectrum of the former is easily interpreted in terms of equilibrium between (IX) and (IXA) with the free hydroxyl of (IX) absorbing at 3635 cm.$^{-1}$ and its free carbonyl contributing to the peak at 1718 cm.$^{-1}$ which is rather broader than most carbonyl bands. Hydrogen-bonding causes the frequency of the greater part of the 3-carbonyl group to fall to 1694 cm.$^{-1}$.

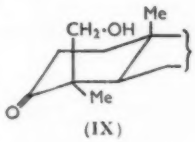


(VIII)

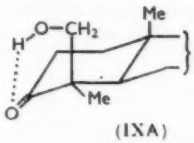


(VIIIA)

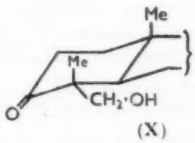
On the other hand, the spectrum of methyl hederagonate is more difficult to interpret. The high-frequency part the hydroxyl absorption is broad with a weak shoulder at about 3630 and its centre at 3602 cm.$^{-1}$, while there is a normal, fairly weak hydrogen-bond band centred at 3540 cm.$^{-1}$. That there is considerable hydrogen-bonding is illustrated by the



(IX)



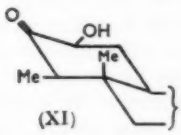
(IXA)



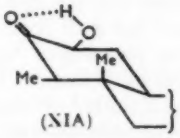
(X)

low 3-carbonyl frequency (1697 cm.$^{-1}$) and absence of free carbonyl near 1710—1715 cm.$^{-1}$ The weak absorption near 3630 cm.$^{-1}$ undoubtedly represents a small amount of free hydroxyl group, and the intramolecular hydrogen-bond might be influenced by the proximity of the π-electron system of the carbonyl group which is in approximately the same plane as the primary hydroxyl system.

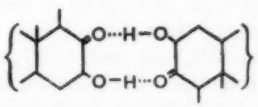
Cerin [12] (XI) belongs to a different class of compound and is included here because it forms an intramolecular hydrogen bond. It is sparingly soluble in carbon tetrachloride, indicating the formation of strong intermolecular hydrogen-bonds in the crystal, and it probably forms dimers similar to those of carboxylic acids (XII). Its hydroxyl spectrum has a " free " band at 3615 cm.$^{-1}$ (a low frequency for a secondary group, due to the presence of the carbonyl group), and two broad hydrogen-bond bands [3491, 3436 cm.$^{-1}$ (weak)]. The first of these is probably due to (XIA) and the second to a small amount of (XII) in solution. In the carbonyl absorption two bands of approximately equal intensity [1715 (free), 1709 cm.$^{-1}$ (bonded)] are just resolved from one another. More examples of compounds with neighbouring ketone and hydroxyl groups must be studied before more conclusions can be drawn about the nature of the interaction.



(XI)



(XIA)

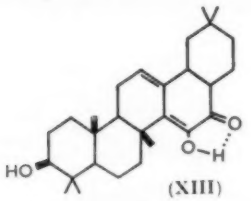


(XII)

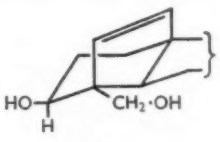
Applications.—The identification of systems involving intramolecular hydrogen-bonds by their infrared absorption has proved useful in the investigation of new compounds in this laboratory. A degradation product (XIII) of A_1-barrigenol [13] has a band at 3629 cm.$^{-1}$ (ε 53) due to the equatorial 3-hydroxyl group, while the bonded enol absorbs at 3415

[12] Corey and Ursprung, *J. Amer. Chem. Soc.*, 1955, **77**, 3668; Brownlie, Spring, Stevenson, and Strachan, *J.*, 1956, 2419.
[13] Cole, Downing, Watkins, and White, *Chem. and Ind.*, 1955, 254.

cm.$^{-1}$ and the conjugated and bonded carbonyl group at 1625 cm.$^{-1}$. A diterpenoid triol [14] isolated from *Beyeria leschenaultii* var. drummondii which has the probable A/B ring system (XIV) and a number of its degradation products show hydroxyl absorption similar to that



(XIII)



(XIV)

of (V), indicating the steric relation of two of the hydroxyl groups. Measurements in this region of the spectrum would assist in the location of hydroxyl groups on ring E of triterpenoids such as treleasegenic acid.[15]

The authors thank Professor D. H. R. Barton, F.R.S., Professor E. R. H. Jones, F.R.S., Dr. T. G. Halsall, and Dr. R. M. Gascoigne who supplied the compounds. The infrared spectrometer was purchased through a generous grant from the Nuffield Foundation. A C.S.I.R.O. Senior Research Studentship (to G. T. A. M.) and a research grant from the University of Western Australia are gratefully acknowledged.

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[*Received, August 25th*, 1958.]

[14] Cole, White, and Woods, unpublished results.
[15] Djerassi and Mills, *J. Amer. Chem. Soc.*, 1958, **80**, 1236.

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243. *Mixed Halides of Phosphorus*(V). *Part II.** *Dichlorotrifluorophosphorane.*

By T. KENNEDY and D. S. PAYNE.

Dichlorotrifluorophosphorane PF_3Cl_2 has been re-examined and its vapour pressure, melting point, infrared spectra, and conductance in acetonitrile are reported. A slow transformation into tetrachlorophosphonium hexafluorophosphate ($[PCl_4^+][PF_6^-]$) has been observed. Vapour-phase hydrolysis leads to high-boiling oxyfluorides and hydrogen chloride.

DICHLOROTRIFLUOROPHOSPHORANE, the product of reaction between phosphorus trifluoride and chlorine, has been examined on several occasions. Moissan [1] and Poulenc [2] established its composition and certain of its physical and chemical properties. Electron-diffraction studies [3] have shown the molecule to have a trigonal bipyramidal structure, with the three fluorine atoms in the equatorial positions and the two chlorine atoms in the polar positions; both the P–Cl (2·05 ± 0·03 Å) and the P–F (1·59 ± 0·03 Å) distances appear somewhat longer than those found in other phosphorus halides. The kinetics of the formation reaction have been briefly reported by Wilson.[4] By the fluorination of phosphorus pentachloride with arsenic trifluoride, Kolditz [5] obtained a compound of identical composition but differing from dichlorotrifluorophosphorane in being clearly ionic in nature, namely tetrachlorophosphonium hexafluorophosphate, $[PCl_4^+][PF_6^-]$. We have

* Part I of this series appeared as "The Reaction between Phosphorus Trichloride and Bromine. Part I," by Harris and Payne, *J.*, 1956, 4613.

[1] Moissan, *Ann. Chim. Phys.*, 1885, **6**, 433, 438.
[2] Poulenc, *Compt. rend.*, 1891, **113**, 75.
[3] Brockway and Beach, *J. Amer. Chem. Soc.*, 1938, **60**, 1836.
[4] Wilson, *ibid.*, 1958, **80**, 1338.
[5] Kolditz, *Z. anorg. Chem.*, 1956, **284**, 144.

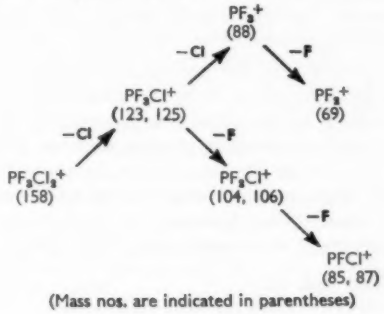
examined the molecular compound PF_3Cl_2 as part of a systematic study of mixed halides of phosphorus(V) and now report further on its chemical and physical properties.

The reaction of phosphorus trifluoride and chlorine in approximately equimolar amounts proceeds slowly in the gas phase at room temperature, but rapidly at lower temperatures in the liquid phase. Irradiation with ultraviolet light failed to accelerate the gas-phase reaction. In every preparation yields were below theoretical and varying amounts of a white solid were obtained. An *X*-ray powder photograph of this solid showed strong lines due to $[PCl_4^+][PF_6^-]$ together with weak lines of $[PCl_4^+][F^-]$. Analysis showed the relative molar amounts to be 9 : 1. On storage the white solid sometimes volatilised and on occasions re-formed as distinct crystals on the walls of the vessel. Separation of the dichlorotrifluorophosphorane from the excess of phosphorus trifluoride always present, and from traces of phosphorus oxyfluoride and silicon tetrafluoride, was accomplished by repeated fractionation at low temperatures in a vacuum line employing taps greased with Florube W. In the initial stages of the work the purification was followed by vapour-pressure checks; later, however, the infrared spectra of gas samples were employed for this purpose.

TABLE 1.

Expt. No.	Temp.	Press. (mm. Hg)	Expt. No.	Temp.	Press. (mm. Hg)	Expt. No.	Temp.	Press. (mm. Hg)	Expt. No.	Temp.	Press. (mm. Hg)
III	−10°	416·33	II	−35°	121·82	I	−45°	73·76	III	−50°	58·79
III	−15	336·84	III	−40	96·70	I	−50	58·35	II	−55	44·19
II	−20	257·25	II	−40	97·70	I	−50	57·39	II	−60	31·00
II	−25	204·69	III	−45	68·39	II	−50	58·90	I	−60	32·10
II	−30	161·68									

The vapour pressure from static measurements is shown in Table 1. The vapour-pressure equation found by the method of least squares, $\log_{10} p_{mm.} = -1228/T + 7{\cdot}264$, gives ΔH for vaporisation = 5·66 kcal. and a value of 20·2 for Trouton's constant. The extrapolated b. p. at 760 mm. is 7·1°. The m. p. lies within the range −125° to −130°. Molecular-weight measurement gave a value of 159 ± 1 at 20° (Calc. for PF_3Cl_2: 158·9), thus establishing the unimolecular nature of the vapour at room temperature. Infrared spectra were obtained at various pressures, a stainless-steel gas cell with potassium bromide windows and lubricated with Kel-F fluorocarbon grease being used. The details of the spectra obtained at 5 mm. pressure are as follows: peaks (cm.$^{-1}$), 932 s, 899 s, 870 s, 675 s, 668 s, 635 s, 564 m, 500 m, 492 m, and 432 w. At 40 mm. and 80 mm., additional peaks at 415 m and 530 s were observed. No attempt has been made to correlate these frequencies with the trigonal bipyramidal model of the molecule. The presence of silicon tetrafluoride and phosphorus oxyfluoride as impurities was clearly apparent through the strong peak of the former at 1024 cm.$^{-1}$ and the triplet of the latter at 1415 cm.$^{-1}$. In connection with later studies a sample of pure dichlorotrifluorophosphorane was examined mass spectroscopically at an ionisation energy of 15 ev; the mass peaks shown in Table 2 were obtained and can be interpreted according to the scheme:



(Mass nos. are indicated in parentheses)

TABLE 2. *Mass spectrum of* PF_3Cl_2 *at* 15 ev.

Mass peak	Strength	Assignment	Mass peak	Strength	Assignment	Mass peak	Strength	Assignment
35	s	Cl^+	87	w	$PClF^+$	123	vs	PF_2Cl^+
37	s	Cl^+	88	s	PF_2^+	125	s	PF_2Cl^+
69	vw	PF_2^+	103	m	PF_2Cl^+	158	vw	$PF_2Cl_2^+$
85	w	$PClF^+$	106	vs	$PF_2Cl^+ + (?)$			

The species with mass number of 106 cannot be exclusively PF_2Cl^+ because of the lower relative peak height of mass 103, which is the adjacent peak corresponding, within the limits of experimental error, to the other chlorine isotope (^{35}Cl). It would be convenient to relate this peak at 106 in part to hydrolysis products such as phosphorus oxyfluoride or silicon tetrafluoride both of mass 104, but the difference in mass number is outside the error of experiment and there is no evidence of hydrogen chloride or of other related fragments being present. Attempts to assign the major part of this strong peak at 106 have therefore not been successful and must await further mass-spectrometric studies of compounds of this type. The ionisation process leads largely to loss of chlorine. Loss of fluorine appears only to occur from a monochloro-fragment, there being no evidence for $PF_2Cl_2^+$ or later fragments in the spectra.

Reference has already been made to a rearrangement leading to the formation of $[PCl_4^+][PF_6^-]$ from PF_3Cl_2; a study of this change and further studies on the pyrolysis reaction in general will be reported later. However, it is appropriate to comment that the speed of the rearrangement of dichlorotrifluorophosphorane to the ionic form can be greatly reduced by rigorous drying of the apparatus, and in the experiments reported in this paper this has always been done.

The molar conductance of a solution of dichlorotrifluorophosphorane in carefully purified acetonitrile at 20° is 9·63 mho cm.$^{-1}$ mole^{-1} at a concentration of 0·04542M and 9·31 mho cm.$^{-1}$ mole^{-1} at 0·09053M. Immediately after preparation of the solutions the conductance increased slightly with time, equilibrium being established only after 1—2 hr. The conductance of liquid dichlorotrifluorophosphorane was found to be less than 10^{-7} mho cm.$^{-1}$.

The hydrolysis of dichlorotrifluorophosphorane vapour with an equimolecular quantity of water gave a high-boiling oxyfluoride together with hydrogen chloride. No evidence in support of the reaction $PF_3Cl_2 + H_2O \longrightarrow POF_3 + 2HCl$ was obtained.

Kolditz [6] has recently discussed the relation of molecular to ionic states in the phosphorus halides. Dichlorotrifluorophosphorane is of particular interest because of the striking difference between the two forms—on the one hand, the ionic $[PCl_4^+][PF_6^-]$, a white solid subliming with decomposition at 135°, with a value of 90·9 mho cm.$^{-1}$ mole^{-1} for the molar conductance in acetonitrile solution at 0·0420M, and on the other, the covalent form with a b. p. of 7·1° and an unusually low m. p. of −125° to −130°, with a molar conductance of *ca.* 9 mho cm.$^{-1}$ mole^{-1} in acetonitrile, the pure liquid being virtually a non-conductor. The evidence presented here supports emphatically the molecular nature of dichlorotrifluorophosphorane, but the conductance data show that in acetonitrile solvolysis is sufficient to bring about limited ion formation. It seems possible that in this medium the rearrangement reported for the gas occurs, but the magnitude of the molar conductance (values should be doubled to compare with $[PCl_4^+][PF_6^-]$) shows that this has not occurred to completion, if at all. The ions responsible for the conductance have not been identified, but a simple ionisation process such as $2PX_5 \rightleftharpoons PX_4^+ + PX_6^-$, where X represents either chlorine or fluorine, following the scheme observed with the simple phosphorus halides in this solvent,[7] would seem to be more favoured than the rearrangement. The slight slow initial increase in conductance with time has been observed before in such systems and may indicate the rate of the ionisation process.

[6] Kolditz, *Z. anorg. Chem.*, 1957, **293**, 147.
[7] Payne, *J.*, 1953, 1052; Harris and Payne, *J.*, 1956, 3038, 4167.

Experimental

Preparation.—Dichlorotrifluorophosphorane is prepared by mixing approximately equal volumes of phosphorus trifluoride and chlorine, care being taken to have a slight excess of phosphorus trifluoride in the final mixture, since this can be removed more easily than excess of chlorine. Phosphorus trifluoride was initially prepared by Hoffman's method,[8] *viz.*, $PCl_3 + AsF_3 \longrightarrow PF_3 + AsCl_3$, but it was later found that phosphorus trifluoride could be prepared more conveniently by the method of Chatt and Williams [9] using zinc fluoride in place of arsenic trifluoride. The phosphorus trichloride was obtained by fractionation of a good commercial sample in a 2-ft. column packed with glass Fenske rings at a reflux ratio of 20 to 1, the fraction of b. p. 74·4—74·5° being retained for use. The crude dichlorotrifluorophosphorane was purified in vacuum by allowing it to distil slowly into a trap immersed in a toluene slush bath (−96°), the impurities passing through being condensed in a liquid-air trap; 12—15 distillations were required to produce pure material. Apiezon and silicone greases were attacked by dichlorotrifluorophosphorane. Florube W and Kel-F greases, being the only ones found to be stable, were used throughout this work.

Analysis.—A known amount of dichlorotrifluorophosphorane was hydrolysed by an excess of 0·1N-sodium hydroxide, the phosphorus being estimated volumetrically, and the chlorine gravimetrically [Found: P, 19·4, 19·3; Cl, 44·2, 43·9; F (by diff.), 36·4, 36·8. Calc. for PF_3Cl_2: P, 19·5; Cl, 44·6; F, 35·9%].

Vapour-pressure Measurements.—These were carried out in an all-glass system, a spiral gauge being used as a null instrument. Considerable difficulty was encountered in obtaining reproducible results; in particular, a change in vapour pressure slowly occurred which could not be explained in terms of reaction with any part of the apparatus or the admission of inadvertent traces of water. The lack of reproducibility may be connected with the ready formation of $[PCl_4^+][PF_6^-]$, since it was observed that samples, even those kept at low temperatures, could not be evaporated without leaving a trace of a white residue, which appeared by the circumstances of its formation and its volatility to be $[PCl_4^+][PF_6^-]$. Satisfactory results for the vapour pressure were eventually obtained by limiting the time taken for equilibrium to be established before a pressure measurement was made to about 30 min. and by employing several highly purified specimens in the course of the complete series of observations. Purity checks were carried out by reference to the infrared spectra, a sensitive detector of the most likely impurities, namely, silicon tetrafluoride and phosphorus oxyfluoride. The homogeneity of the sample was further checked by the successive removal of the vapour phase and the separate examination of these fractions.

Molecular-weight Measurements.—These were carried out by using a vapour-density bulb fitted with a tap greased with Florube W, in combination with the spiral gauge pressure-measuring system.

Conductance Experiments in Acetonitrile.—These were carried out in an all-glass cell fitted with a pair of smooth platinum electrodes (area *ca.* 1 cm.^{2}, cell constant 0·324 cm.$^{-1}$) and maintained at a constant temperature by means of a water-bath. Solutions for conductance measurements were prepared by passing a known weight of pure sample in a slow stream of dry nitrogen into a weighed amount of solvent. The conductance was measured by a Mullard conductance bridge (Type E7566). Readings were taken immediately the dichlorotrifluorophosphorane had passed into solution, and observations on the variation of bridge reading with time were then carried out. The acetonitrile was purified essentially as by Smith and Witten's method.[10] However, immediately before use, the solvent was distilled *in vacuo* from *ca.* 20° to −183°. This served to remove phosphoric oxide, traces of which sublimed over from the desiccating agent during distillation at ordinary pressures. The purified material had a specific conductance of *ca.* 10^{-6} mho cm.$^{-1}$. The conductance of liquid dichlorotrifluorophosphorane was measured in an all-glass cell with small platinum electrodes, the cell being specially constructed to deal with small quantities of volatile material. Measurements were made by using the Mullard bridge.

Mass-spectrometer Studies.—These were carried out by use of a Metro Vick MS2 instrument. Measurements were made at 15 ev and at a pressure of 10^{-6} mm., samples being transferred to the apparatus by means of bulbs fitted with magnetic break seals.

[8] Hoffman, "Inorganic Syntheses," McGraw-Hill, New York, 1953, Vol. IV, 140.
[9] Chatt and Williams, *J.*, 1951, 3065.
[10] Smith and Witten, *Trans. Faraday Soc.*, 1951, **47**, 1304.

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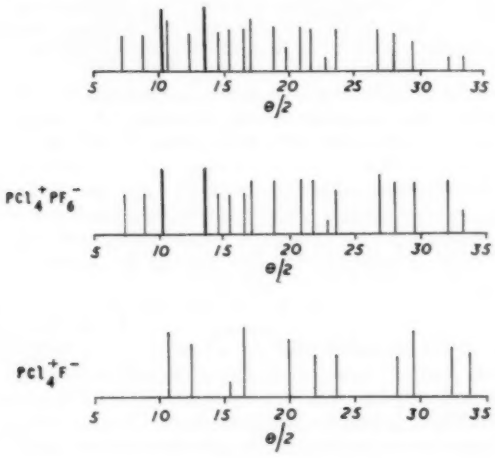
Infrared Spectra.—A Unicam double-beam instrument (S.P. 100) was used. Samples were contained in a stainless-steel gas cell of 10 cm. path length, fitted with KBr windows, and of capacity approximately 0·2 l. Spectra were observed at a number of pressures (measured by the spiral-gauge system already described).

Melting Point.—This was measured by surrounding a solidified sample of pure dichlorotrifluorophosphorane with an *iso*pentane slush bath (−160·5°) and allowing the bath temperature to rise slowly until the solid appeared just to melt, the procedure being repeated three times to obtain a reproducible range of melting.

The *X*-ray powder diagram of the solid obtained on storage of dichlorotrifluorophosphorane, taken with Cu-K_α radiation in a camera of diameter 11·45 cm., is shown below. Data for $[PCl_4^+][PF_6^-]$ [5] and $[PCl_4^+][F^-]$ [11] are shown for comparison.



Reaction with Water Vapour.—This experiment was carried out at room temperature (20°). A bulb of approximately 300 ml. capacity was filled to the pressure corresponding to the vapour pressure of water at the temperature of the experiment with dichlorotrifluorophosphorane. This was then removed, and the bulb refilled with water vapour to the same pressure by allowing it to come to equilibrium with liquid water. The two were then brought into contact, and the vapour phases allowed to react, the pressure of the system being observed by using the spiral-gauge system. After an initial pressure variation, the final pressure of the system corresponded to no net change in the volume of vapour present. The products of the reaction, present in part as droplets of liquid, were divided into a non-volatile and a volatile fraction; the former contained, as shown by examination of the hydrolysed material, only phosphorus and fluorine, the latter only chlorine. The evidence thus supports the reaction $PF_3Cl_2(g) + H_2O(g) \longrightarrow 2HCl(g) + (POF_3)_x(l)$.

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CHEMISTRY DEPARTMENT,
THE UNIVERSITY, GLASGOW, W.2.

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[11] Kolditz, *Z. anorg. Chem.*, 1956, **286**, 307.

244. *Reactivities of Aromatic Hydrocarbons. Part II.*[1] *Chlorination.*

By S. F. Mason.

The second-order rate constants for the reaction of molecular chlorine with benzene, diphenyl, naphthalene, and phenanthrene in acetic acid have been measured at 15, 20, 25, and 30° c, and the energies of activation and the frequency factors have been determined. The frequency factors decrease as the reactivity of the hydrocarbon increases, suggesting, from a consideration of the solvation entropy, that the Wheland intermediate is formed more completely in the transition state for a given reaction the more reactive the hydrocarbon. The effects of the atom localisation, electron interaction, and solvation energies of the transition state upon the course of aromatic substitution are discussed.

In connection with the theory of aromatic substitution,[1] the frequency factors for the reaction of a series of aromatic hydrocarbons with an electrophilic reagent of high orientational selectivity were required. The molecular halogens are highly selective reagents,[2] and although the kinetics of aromatic bromination are complex,[3] the reactions of chlorine with aromatic compounds have been found generally [4-9] to be of the simple kinetic form $-d[Cl_2]/dt = k_2[ArH][Cl_2]$. The rates of chlorination of benzene, diphenyl, naphthalene, and phenanthrene in acetic acid at 15, 20, 25, and 30° have now been measured, and the energies of activation and the frequency factors have been calculated from the experimental data (Table 1). In the chlorination of the polycyclic hydrocarbons, catalysis by hydrogen chloride generated in the course of the reaction was observed, in agreement with some previous investigations.[6,9] Accordingly, the quoted rate constants are averages calculated from the first half-life of the reaction, though the kinetic runs were taken to the third or fourth half-life.

Table 1. *The second-order rate constants at* 15, 20, 25, *and* 30 ± 0·05° c *for the reaction of benzene, diphenyl, naphthalene, and phenanthrene with chlorine in acetic acid; the energies of activation* (E_a) *and the logarithms of the frequency factors* (log PZ).

Hydrocarbon	[Ar] (M)	[Cl_2] (M)	K_{15} (l. mole^{-1} sec.$^{-1}$)	K_{20}	K_{25} [b]	K_{30}	E_a (kcal./mole)	log PZ
Benzene	0·5	0·04	3·8 × 10^{-7}	6·8 × 10^{-7}	1·2 × 10^{-6} [c]	2·2 × 10^{-6}	20	9
Diphenyl	0·2	0·04	3·32 × 10^{-4}	5·19 × 10^{-4}	8·62 × 10^{-4}	1·25 × 10^{-3}	14·8	7·8
	0·1	0·02	—	5·25 × 10^{-4}	—	1·33 × 10^{-3}	—	—
Naphthalene	0·04	0·004	3·72 × 10^{-3} [a]	5·21 × 10^{-3}	7·30 × 10^{-3} [d]	1·03 × 10^{-1}	11·5	7·3
Phenanthrene	0·01	0·002	3·10 × 10^{-1}	4·55 × 10^{-1}	—	—	—	—
	0·005	0·002	3·24 × 10^{-1}	4·45 × 10^{-1}	5·91 × 10^{-1}	7·94 × 10^{-1}	10·5	7·4

[a] Compare 7·0 × 10^{-3} at 15·3°, ref. 6. [b] The results of refs. 5 and 8 are not comparable with the present data, the former owing to the volatilisation of chlorine,[6] and the latter because only pseudo-first-order rate constants are given. [c] Compare 1·48 × 10^{-6} at 24°, ref. 6; 1·54 × 10^{-6}, ref. 9; and 1·1 × 10^{-6}, ref. 12. [d] Compare 10·5 × 10^{-3} at 24°, ref. 6.

The results show (Table 1) that the energies of activation increase as the reactivities of the aromatic hydrocarbons towards chlorine fall, and that the frequency factors, although showing less variation, tend to larger values as the reactivities of the hydrocarbons decrease. Since the free energies of activation in a series of aromatic hydrocarbons increase with the atom localisation energy ($E_L\beta^{-1}$) of the most reactive position in a variety of substitution

[1] Part I, *J.*, 1958, 4329.
[2] Brown and Stock, *J. Amer. Chem. Soc.*, 1957, **79**, 1421.
[3] Robertson, de la Mare, and Johnston, *J.*, 1943, 276.
[4] Orton and King, *J.*, 1911, 1369.
[5] Lauer and Oda, *Ber.*, 1936, **69**, 1061.
[6] de la Mare and Robertson, *J.*, 1943, 279.
[7] Robertson, *J.*, 1954, 1267.
[8] Dewar and Mole, *J.*, 1957, 342.
[9] Brown and Stock, *J. Amer. Chem. Soc.*, 1957, **79**, 5175.

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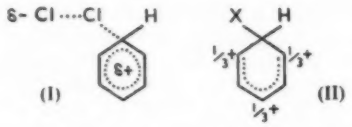
reactions,[1,8,10] it is probable that the transition state for aromatic substitution (*e.g.*, I) lies on a potential energy curve connecting the reactants with the Wheland intermediate [11] (*e.g.*, II; X = Cl). There are indications [1,8,10] that the intermediate is formed the more



(I) (II)

completely in the transition state the greater the orientational selectivity of the attacking reagent, the degree of formation being substantial in aromatic substitution with molecular halogens. The effect of electrolytes on the rates of aromatic chlorination indicates [9,12] that the electrophilic reagent is molecular chlorine, so that the formation of the transition state involves the separation of charge, resulting in an increase in the free energy of solvation. For electrophilic substitution the Wheland intermediate is an odd alternant carbonium ion with the positive charge delocalised over the starred atoms [*e.g.*, one-third of the charge at the *ortho*- and *para*-positions in (II), according to the Hückel approximation], and in a series of aromatic hydrocarbons the charge in the corresponding intermediates is dispersed to differing degrees. The free energy of solvation, particularly that due to the Born charging process,[13] accordingly varies from one transition state to another. For the fully formed intermediate the charging energy (ΔG_S) is given by the equation

$$\Delta G_S = -\sum_r \sum_s q_r q_s (1 - 1/D)/2R_{rs} \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where q_r, q_s, are the fractional positive charges on atoms r and s, separated by the distance R_{rs}, and D is the dielectric constant of the solvent. If the intermediate (*e.g.*, II) is formed to a degree, d in the transition state (*e.g.*, I), and the fractional positive charge, $d+$, is delocalised over the starred atoms in the transition state, as in the intermediate, eqn. (1) becomes, by considering only the more important one-centre terms,

$$\Delta G_S^{\ddagger} = -\sum_r q_r^2 d^2 (1 - 1/D)/2R \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where R is the effective radius of a positively charged carbon atom. The derivative of the free energy of solvation ($\Delta G_S^{\ddagger}$) with respect to temperature then gives the entropy of the solvation of the transition state due to the charging process ($\Delta S_S^{\ddagger}$), namely,

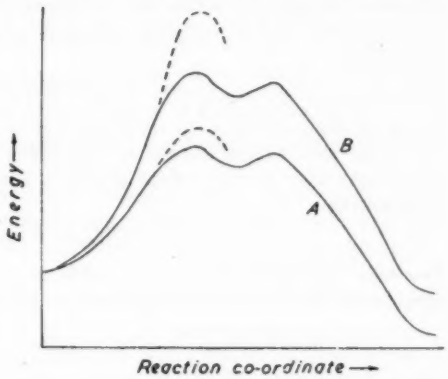
$$\Delta S_S^{\ddagger} = \sum_r q_r^2 d^2 (\mathrm{d} \ln D/\mathrm{d}T)/2RD \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

If, for a given substitution, the degree of formation of the intermediate in the transition state (d) is constant in the series of aromatic hydrocarbons, the frequency factor for the reaction should increase, by eqn. (3), as the summed squares of the charges ($\sum_r q_r^2$) fall, since the temperature coefficient of the dielectric constant is a negative quantity for liquids, apart from a few cases, including acetic acid,[14] where the coefficient is positive at temperatures close to the freezing point. If variable in the series of aromatic hydrocarbons for a given reaction, the degree of formation of the intermediate in the transition state should increase as the atom localisation energy falls, as, in any given case, the path of lowest activation energy should pass closer to the intermediate the lower the energy required to form the latter (Fig.). Since the separation of charge in the transition state is larger the more completely the intermediate is formed, the frequency factor should then

[10] Dewar, Mole, and Warford, *J.*, 1956, 3581.
[11] Wheland, *J. Amer. Chem. Soc.*, 1942, **64**, 900.
[12] de la Mare and Hassan, *J.*, 1958, 1519.
[13] Hush and Blackledge, *J. Chem. Phys.*, 1955, **23**, 514; Hoijtink, de Boer, van de Meij, and Weijland, *Rec. Trav. chim.*, 1956, **75**, 487.
[14] Philippe and Piette, *Bull. Soc. Chim. Belges*, 1955, **64**, 600.

fall with the atom localisation energy. The frequency factors for the chlorination of the aromatic hydrocarbons studied are of the order 10^7—10^9 (Table 1), suggesting that the transition states are more polar than the reactants, and the trend of the factors in the series indicates that the separation of charge in the transition state is larger the more reactive the hydrocarbon.

These conclusions are unaffected by the assumption of a Hückel distribution of positive charge in the transition state. Given a uniform degree of formation of the Wheland intermediate in the transition state, any mode of charge dispersion would require the larger hydrocarbons to have the higher frequency factors. Steric factors could account for the observed trend in the frequency factors, namely, *peri*-hindrance to substitution in naphthalene and phenanthrene, and *ortho-ortho'*-interference in diphenyl, but if the



The course of substitution in (A) a reactive and (B) an unreactive aromatic hydrocarbon.

– – – – – *The potential energy curve connecting the reactants with the Wheland intermediate.*

——— *The potential energy curve connecting the reactants with the products through the transition state.*

transition state resembles the Wheland intermediate steric effects are not to be expected, as the carbon atom under attack assumes a near tetrahedral configuration with the entering and leaving groups out of the plane of the nucleus.

The dielectric constant of acetic acid over part (16—20°) of the temperature range studied has a positive temperature coefficient,[14] probably due to an extensive breakdown in the structure of the liquid for a small temperature rise above the freezing point. Curved Arrhenius plots for reactions involving a separation of charge in the transition state might be expected in solvents of this nature for a temperature range near to the freezing point (eqn. 3). The Arrhenius plots obtained for the chlorination of the aromatic hydrocarbons were all reasonably linear, the kinetic effect of the positive temperature coefficient of the dielectric constant being probably rather small. In order to allow for the breakdown of the solvent structure by the reactant solutes, as manifest in the depression of the freezing point, a number of kinetic runs were made below the melting point of the pure solvent, at 15°. The more dilute solutions, *e.g.*, phenanthrene at 0·005M, were slightly supercooled at this temperature, but no crystallisation of the solvent was observed during the brief kinetic run (half-life of ~10 min.).

The observed variation of the frequency factors for chlorination of the series of aromatic hydrocarbons studied has a bearing on the interpretation of the linear relations which have been found between the free energy of activation and the atom localisation energy in a number of aromatic substitutions.[1,8,10] The variation of the frequency factors suggests that, for a given reaction, the Wheland intermediate is formed in the transition state to a degree (d) which is approximately proportional to the reactivity of the hydrocarbon. The observed relations between $\Delta G^{\ddagger}$ and $E_L\beta^{-1}$ require that any variations in d should be of this form, as otherwise those relations would not be linear. Thus, the reaction co-ordinate leaves the potential energy curve connecting the reactants with the Wheland intermediate at an earlier stage the larger the atom localisation energy (*e.g.*, cases *A* and *B*,

Fig.). The apparent β value obtained from the correlation between $\Delta G^{\ddagger}$ and $E_L\beta^{-1}$ for a given reaction is a composite quantity, therefore, expressing not only an average degree of formation of the Wheland intermediate in the transition state for a series of hydrocarbons, but also a range of variation of d in the series and a variable solvation energy of the transition state.

The solvation of the transition state, whilst affecting the entropy of activation for electrophilic aromatic substitution (eqn. 3), may not have a great influence upon the energy of activation, as a more detailed treatment suggests that π-electron energy terms, not considered in the simple Hückel theory, partly compensate the variations in the solvation energy of the transition state in the substitutions of a series of aromatic hydrocarbons. By using a simplified self-consistent field method,[15] with the Hückel molecular orbitals as a base, the π-electron energy difference (E_π) between an aromatic hydrocarbon (*e.g.*, benzene) and the corresponding Wheland intermediate (*e.g.*, II) is given [15] by the expression

$$E_\pi = E_L + E_B \pm E_C \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

E_C being negative for the carbonium ion and positive for the radical intermediate. E_L, the atom localisation energy of the Hückel theory, arises from the delocalisation of π-electrons over a σ-core field which is less extensive in the intermediate than in the hydrocarbon

$$E_L = 2[\textstyle\sum'_{r>s} P_{rs(\mathrm{Int})} - \sum'_{r>s} P_{rs(\mathrm{ArH})}]\beta \quad . \quad . \quad . \quad . \quad . \quad (5)$$

The bond repulsion energy, E_B, is due to the smaller probability that pairs of electrons shall be found on neighbouring atoms in the intermediate than in the hydrocarbon

$$E_B = 1/2[\textstyle\sum_r^{st}\sum_s^{un} P_{rs}^2(\gamma_{12} - \gamma_{rs})_{\mathrm{Int}} - \sum_{r>s}' P_{rs}^2(\gamma_{12} - \gamma_{rs})_{\mathrm{ArH}}] \quad . \quad . \quad . \quad . \quad (6)$$

where P_{rs} refers to the mobile bond order between the atoms r and s, the sums $\sum^{st}$, $\sum^{un}$, and $\sum'$ being taken over the starred, the unstarred, and neighbouring atoms, respectively, and γ_{rs} is the electron repulsion integral between the atoms r and s, ArH referring to the hydrocarbon and Int to the corresponding Wheland intermediate. The charge dispersal energy, E_C, arises from the lower probability that a pair of electrons shall be situated on a given atom in the delocalised than in the fixed bond state of the intermediate

$$E_C = 1/2 \textstyle\sum_{r>t}^{st} C_{or}^2 C_{ot}^2 (\gamma_{11} - \gamma_{rt}) \quad . \quad . \quad . \quad . \quad . \quad (7)$$

where C_{or} is the coefficient of the atom r in the non-bonding molecular orbital on the intermediate. Values of the various π-electron energy terms for a number of Wheland intermediates in aromatic substitution are given in Table 2.

In electrophilic substitution the transformation of an aromatic hydrocarbon into a transition state resembling a partly formed Wheland intermediate involves a change in π-electron delocalisation energy proportional to the degree of formation of the intermediate, d, but changes in electron interaction and solvation energy proportional to d^2. Thus the variation in the free energy of activation in a series of aromatic hydrocarbons for a given reaction should be given by the equation

$$\Delta G^{\ddagger} = dE_L + d^2(\Delta G_S + E_B - E_C) + \mathrm{Constant} \quad . \quad . \quad . \quad (8)$$

The charge-dispersal energy (E_C) has the form of a charging energy. It may be considered (eqn. 7) as the difference between the charging energy of two charges, C_{or}^2 and C_{ot}^2, when on a common centre and when on their proper centres, the atoms r and t, summed over all pairs of charges. The charge-dispersal energy and the solvation energy due to the charging process (eqns. 1 and 2) are, therefore, related. In the series of aromatic hydrocarbons E_C increases as $\sum_r q_r^2$ falls (Table 2), and the changes in the charge-dispersal and the solvation

[15] Brickstock and Pople, *Trans. Faraday Soc.*, 1954, **50**, 901.

TABLE 2. *The atom-localisation ($E_L\beta^{-1}$), charge-dispersal (E_C), and bond-interaction (E_B) energies, and the summed squares of the positive charges ($\sum_r q_r^2$), calculated according to the Hückel approximation, of some Wheland intermediates in aromatic substitution. The hyperconjugation energies of the cations ($E_{HC}\beta^{-1}$), and the delocalisation energies of the corresponding aryl methyl systems ($E_D\beta^{-1}$).*

Hydrocarbon	Position	$E_L\beta^{-1}$	E_B [a] (kcal./mole)	E_C [b] (kcal./mole)	$\sum_r q_r^2$	$E_{HC}\beta^{-1}$ [c]	$E_D\beta^{-1}$
Benzene		−2·536	−6·7	19·5	0·333	0·75	0·722
Diphenyl	2	−2·400	−8·9	26·2	0·227	—	0·767
	4	−2·447	−10·4	26·2	0·227	—	0·756
Naphthalene ...	1	−2·299	−10·6	23·3	0·289	0·67	0·812
	2	−2·480	−8·6	22·3	0·313	—	0·744
Phenanthrene...	1	−2·318	−13·6	26·5	0·296	—	0·802
	9	−2·299	−12·0	23·1	0·319	0·66	0·812
Anthracene ...	9	−2·013	−18·3	27·1	0·220	0·58	0·951

[a] Calculated from eqn. (5) with[15] $\gamma_{12} = 168{\cdot}3$, $\gamma_{14\,(etc)} = 113{\cdot}0$ kcal./mole, and the point-charge approximation for larger distances. [b] Calculated from eqn. (6) with[15] $\gamma_{11} = 242{\cdot}7$, $\gamma_{12} = 125{\cdot}9$ kcal./mole, and the point-charge approximation for larger distances. [c] Quoted from ref. 16.

energies, in part, are mutually compensating irrespective of the degree of formation of the intermediate.

Attention has been drawn recently[16] to another π-electron energy term which partly compensates for the changes of solvation energy in a series of Wheland carbonium-ion intermediates, namely, the Coulombic stabilisation due to the movement of the π-electrons in the field of the carbon atons carrying a positive charge. If the intermediate is formed to a degree, d, in the transition state, the Coulombic stabilisation energy of the latter, E_E, is given by

$$E_E = m(d - \sum_r q_r^2 d^2)\beta \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (9)$$

where q_r, the net positive charge on atom r, is equal to C_{or}^2, and m is a constant which has been given the values[17,18] of unity and 1·4. The Coulombic stabilisation energy of the transition state increases (eqn. 9) in proportion as the solvation energy falls (eqn. 2). The overall effect of the charge dispersal, Coulombic, and solvation energies of the transition state upon the relative reaction rates of a series of hydrocarbons may be small, therefore, though the solvation energy is manifest, because it is a free-energy term, in the relative frequency factors.

The linear relations between the free energy of activation and the atom localisation energy in a series of hydrocarbons observed in a number of substitution reactions[1,8,10] can be accounted for if, as the relative frequency factors suggest (Table 1), the degree of formation of the Wheland intermediate in the transition state is approximately proportional to the reactivity of the hydrocarbon. The partial compensation between the solvation energy and the charge dispersal and Coulombic energies of the transition state has the effect that the atom localisation energy remains the most important single variable governing the relative reactivities of a series of hydrocarbons for a given substitution, the bond repulsion energy becoming important also when the average degree of formation of the intermediate in the transition state is large (eqn. 8). The bond repulsion energy (E_B) tends to larger values as the atom localisation energy ($E_L\beta^{-1}$) falls (Table 2), and so the former should not lead to marked irregularities in the correlations between $\Delta G^\ddagger$ and $E_L\beta^{-1}$. However, the values of E_B available account for an otherwise anomalous relative reactivity. Naphthalene and phenanthrene have the same atom localisation energies for the most reactive positions, but the reduction of electron repulsion (E_B) on change from the hydrocarbon to the intermediate is larger in the latter than in the former (Table 2), in accord with the greater reactivity of phenanthrene.

[16] Mackor, Hofstra, and van der Waals, *ibid.*, 1958, **54**, 66.
[17] Wheland and Mann, *J. Chem. Phys.*, 1949, **17**, 264.
[18] Muller, Pickett, and Mulliken, *J. Amer. Chem. Soc.*, 1954, **76**, 4770.

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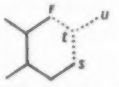
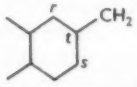
The apparent β values obtained from the slopes of the relations between $\Delta G^{\ddagger}$ and $E_L\beta^{-1}$ in a series of aromatic hydrocarbons for the various substitution reactions are less satisfactorily explained. An empirical upper limit of −35 kcal./mole for such apparent β values is provided by the relation between the ionisation constants [18] of a series of aromatic hydrocarbons in anhydrous hydrofluoric acid and $E_L\beta^{-1}$, since the cations formed probably have the structures of the corresponding Wheland intermediates.[16] The apparent β values derived from rate studies should be smaller, as the intermediate is incompletely formed in the transition state and the degree of formation in a series of hydrocarbons would appear to be proportional to the reactivity of the hydrocarbon. However, the apparent β value obtained [1] from the reaction of a series of hydrocarbons with chlorine in 3 : 1 carbon tetrachloride–acetic acid [8] is −36 kcal./mole. Further, the relative enthalpies of activation for the reaction with chlorine in acetic acid, which are given by the relative energies of activation (Table 1), as each hydrocarbon was investigated between the same temperature limits, correlate with the atom localisation energies (Table 2) to give an apparent β value of −48 kcal./mole, whilst the enthalpies of ionisation, like the free energies, give a value of −35 kcal./mole, since no differential entropy of ionisation was observed in the series of hydrocarbons studied.[19]

Two factors may account for the large apparent β values obtained from the aromatic halogenation series. First, the cations of the hydrocarbons are stabilised by hyperconjugation between the $>CH_2$ group and the π-electron system of the ion [18] (*e.g.*, II; X = H), whilst the transition state in the substitution reaction is less stabilised by hyperconjugation as the entering group is a halogen and not a hydrogen atom. The calculated hyperconjugation energies [16] of the cations of the aromatic hydrocarbons increase with the atom localisation energy (Table 2), so that these two energy terms mutually compensate to some degree in the hydrocarbons. Thus, if hyperconjugation is not explicitly considered in the correlations, the free energies of ionisation of the hydrocarbons appear to be less strongly dependent upon the atom localisation energies than the free energies of activation for a substitution with a transition state in which the Wheland intermediate is largely formed. Secondly, in the product of an aromatic halogenation the halogen atom conjugates more strongly with the nucleus the more reactive is the position substituted. An approximate measure of the conjugating power of a nuclear position for a given substituent is afforded by the delocalisation energy ($E_D\beta^{-1}$) of the corresponding arylmethyl radical or ion (*e.g.*, benzyl) additional to that of the nucleus (*e.g.*, benzene), an energy term which increases in proportion as the atom localisation energy falls (Table 2). In an aromatic halogenation the energy of the partly formed carbon–halogen bond should lower the energy of the transition state, and the more reactive the position substituted, the stronger the conjugation across the partial bond, and the more stable should be the transition state. The effects of both hyperconjugation in the transition state and the conjugation of the partly bonded substituent are to accentuate the dependence of the relative reactivities of a series of hydrocarbons on the atom localisation energy, and they both help to account for the large apparent β values derived from the aromatic halogenations.

(III) 



(IV)

The interdependence of the atom localisation energy (E_L) of a given position in an aromatic hydrocarbon, the hyperconjugation energy of the corresponding cation (E_{HC}), and the extra delocalisation energy of the corresponding arylmethyl system (E_D), may be accounted for by the perturbation method of Dewar.[20] The localisation energy of the atom *t* in the hydrocarbon (III) is given [20] by

$$E_L = 2(C_r + C_s)\beta \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (10)$$

[19] Mackor, Hofstra, and van der Waals, *Trans. Faraday Soc.*, 1958, **54**, 186.
[20] Dewar, *J. Amer. Chem. Soc.*, 1952, **74**, 3341.

where C_r and C_s are the coefficients of the non-bonding molecular orbital in the corresponding Wheland intermediate at the atoms r and s adjacent to t. If the H_2 pseudo-atom of the corresponding cation is the atom u in (III), and if, for the purposes of illustration, all Coulomb integrals and all resonance integrals are taken to be equal, the hyperconjugation energy of the cation is

$$E_{HC} = 2(1 + C_r + C_s)\beta \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (11)$$

The extra delocalisation energy of the corresponding arylmethyl system (IV) is given, similarly, by

$$E_D = 2(1 - C_r' - C_s')\beta \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (12)$$

where C_r', C_s', are the values C_r and C_s assume after the renormalisation of the non-bonding molecular orbital to include the coefficient of the orbital at the exocyclic atom. Thus E_L, E_{HC}, and E_D are interrelated (equations 10—12) through the coefficients C_r and C_s. These connections indicate that a correlation between the reactivities of a series of hydrocarbons and their atom localisation energies does not necessarily imply that the transition state resembles the Wheland intermediate. If the product of an aromatic substitution contains a highly conjugated substituent, and if the transition state resembles the product, an accidental correlation between relative reactivity and the atom localisation energy might be found, owing to the connection between E_L and E_D (eqns. 10 and 12).

The apparent β values obtained from the slopes of the relations between $\Delta G^{\ddagger}$ and $E_L\beta^{-1}$ in a series of aromatic hydrocarbons, in general, become smaller the less selective the attacking reagent,[1,8,10] suggesting that the transition state more resembles the reactants the more reactive the substituting agent.[8,10] The present results indicate that the transition state more nearly resembles the Wheland intermediate the more reactive the hydrocarbon, which, at first sight, is surprising, since there is no distinction in principle between the reactants, the hydrocarbon, and the substituting reagent. However, the lower the atom localisation energy of an aromatic hydrocarbon the more nearly the intermediate resembles the hydrocarbon itself in regard to the important variable determining the course of reaction, *i.e.*, energy, so that in this respect the present conclusions do not require the non-equivalence of the reactants in aromatic substitution.

Experimental

Materials and Rate Measurements.—These were as in Part I. The formula $k_2 = 2{\cdot}303\{\log_{10} b(a - x)/a(b - x)\}/t(a - b)$ was used to calculate second-order rate constants, where a and b are the molarities of aromatic hydrocarbon and of chlorine, respectively, and x is the molarity of chlorine consumed after a time t. The following is an example of a typical run, illustrating the catalytic effect of hydrogen chloride generated during the course of the reaction and the reproducibility of rate constants calculated from the first half-life (about ± 7 units in the last significant figure for a standard set of reaction conditions). Naphthalene (0·04M) and chlorine (0·00437M) reacted at 20°; samples (10 ml.) were titrated against 0·001N-sodium thiosulphate.

Time (sec.)	0	83	200	330	440	520	660	780
Titre (ml.)	43·7	33·8	26·5	20·7	16·2	12·7	9·8	7·8
10^2k_2 (l. mole^{-1} sec.$^{-1}$)	—	5·15	5·28	5·18	5·38	5·48	5·67	5·60

The author is indebted to Dr. J. Pople for the bond orders of the 1-phenylallyl system, to Dr. F. Sumner for the coefficients, levels, and band orders of the other Wheland intermediates and of phenanthrene, to Dr. H. H. Greenwood for the coefficients and levels of the diphenylyl- and phenanthryl-methyl systems, and to Dr. J. H. Ridd for discussion of the present results.

Chemistry Department, The University, Exeter. [*Received, June 20th*, 1958.]

245. *The Electronic Spectra of N-Heteroaromatic Systems. Part I.* The $n \longrightarrow \pi$ Transitions of Monocyclic Azines.*

By S. F. Mason.

The positions and the intensities of the band in the visible and the ultraviolet spectra of monocyclic azines due to the promotion of an electron from a lone-pair nitrogen orbital to a π-orbital of the ring have been measured for the vapour phase for *cyclo*hexane and aqueous solutions. The frequency of the band is determined primarily by the energy of the benzene-like lowest unoccupied π-orbital of the azine and by ground-state interaction between lone-pair orbitals on different nitrogen atoms. The intensities of the $n \longrightarrow \pi$ bands of the azines increase with the "*s*" character of the lone-pair nitrogen orbitals, but the frequencies of the bands are not greatly affected, owing to orbital-following in the transition.

The ultraviolet and visible absorption of monocyclic azines have been examined by a number of workers,[1-9] who find that these compounds give an absorption band which has no counterpart in the spectrum of benzene. From the relatively low intensity of the band and its shift to higher frequencies with change from non-polar to polar solvents, it has been concluded [10-12] that the band arises from the transmission of a non-bonding electron from a lone-pair orbital of a nitrogen atom to a π-orbital of the ring. The theory of the $n \longrightarrow \pi$ transition in pyridine and the diazines has been discussed,[13] but the $n \longrightarrow \pi$ spectra of the azines as a whole have not been considered in detail. To obtain data for a more comprehensive treatment, the $n \longrightarrow \pi$ transitions of all of the known monocyclic azines have now been examined in the vapour and in *cyclo*hexane and aqueous solutions, the results being recorded in the Table and the Figures.

The $n \longrightarrow \pi$ transitions of the monocyclic azines are weak, possessing oscillator strengths in the range 0·003—0·021 (Table). The transitions are not forbidden by symmetry, however, as strong 0–0 vibrational bands have been identified in the spectra of the vapour of pyridine,[5] pyrimidine,[3] pyrazine,[9] and *sym*-tetrazine.[14] The weakness of the intensity may be ascribed to three main factors. First, the lone-pair and the π-orbitals of an azine are concentrated in different regions of space, and transitions requiring large changes in the position of an electron are improbable.[11] Secondly, only the *s*-component of the *s*–*p* hybrid lone-pair orbital can contribute to the transition moment,[13] since $p_\sigma \longrightarrow p_\pi$ transitions are forbidden. The third factor, the small overlap between π-electron charge distributions [13] of the ground and the excited state, is not of great importance. This factor leads only to a fourfold reduction in the intensity of the $n \longrightarrow \pi$ transition of pyridine,[13] and it is less significant in the case of the polyaza-compounds where the migration of charge from nitrogen to carbon in the transition is smaller, or, as in the case of *sym*-tetrazine, absent.

* In this series of papers aza-substitution refers to *replacement* of a CH-member of a benzene ring by a nitrogen atom; otherwise the term substitution has its usual significance.

[1] Curtius, Darapsky, and Müller, *Ber.*, 1907, **40**, 84.
[2] Koenigsberger and Vogt, *Physikal. Z.*, 1913, **14**, 1269.
[3] Uber, *J. Chem. Phys.*, 1941, **9**, 777.
[4] Halverson and Hirt, *ibid.*, 1951, **19**, 711.
[5] Rush and Sponer, *ibid.*, 1952, **20**, 1847.
[6] Stephenson, *ibid.*, 1954, **22**, 1077.
[7] Hirt, Halverson, and Schmitt, *ibid.*, 1954, **22**, 1148.
[8] Mason, *Chem. Soc. Special Publ.*, 1955, **3**, 139.
[9] Ito, Shimada, Kuraishi, and Mizushima, *J. Chem. Phys.*, 1957, **26**, 1508.
[10] Kasha, *Discuss. Faraday Soc.*, 1950, **9**, 14.
[11] Platt, *J. Chem. Phys.*, 1951, **19**, 101.
[12] McConnell, *ibid.*, 1952, **20**, 700.
[13] Orgel, *J.*, 1955, 121.
[14] Part IV, *J.*, 1959, 1263.

The $n \longrightarrow \pi$ transitions of the azines show a small red shift on change from vapour to *cyclo*hexane solution (Table), which can be ascribed [15] to the momentary polarisation of the hydrocarbon solvent by the transition dipole of the azine solute. On change from *cyclo*hexane to aqueous solution there are considerable blue shifts (Table), and on formation of a cation in acid solution the $n \longrightarrow \pi$ bands of the azines undergo further blue shifts or disappear (Fig. 1). In aqueous solution the lone-pair electrons of the azines are engaged in hydrogen-bonding, and the promotion of such an electron to a π-orbital requires the provision of additional energy to weaken or break the hydrogen bonds. In an azine cation the lone-pair electrons either bind a proton or are held more strongly in their orbital by inductive and electromeric effects originating from a charged centre elsewhere in the molecule. The blue shifts of the $n \longrightarrow \pi$ bands observed on changing from *cyclo*hexane to aqueous solution should provide a measure of the electron-donating capacity of the azines. The shifts vary widely, ranging from 1000 cm.$^{-1}$ for *sym*-tetrazine to 3900 cm.$^{-1}$ for pyridazine, and, in general, the shifts are larger the more basic the azine (Table), apart

The frequencies (ν) *and the oscillator strengths* (f) *of the* n $\longrightarrow \pi$ *transitions of the monocyclic azines in the vapour and in* cyclo*hexane and aqueous solution. The red shifts of the band origins* (ν_{0-0}) *in the vapour phase and the band maxima* ($\nu_{max.}$) *in* cyclo*hexane solution relative to pyridine* ($\Delta\nu_{obs}$), *and the theoretical red shifts due to the lowering of the energy of the unoccupied* π*-orbitals on aza-substitution* ($\Delta\nu_\pi$) *and to ground state interaction between the lone-pair orbitals* ($\Delta\nu_n$). *The ionisation constants of the azines* (pK_a), *and the blue shift of the band maxima observed on change from* cyclo*hexane to aqueous solution* ($\nu_{H_2O}-\nu_{C_6H_{12}}$). *Values in parentheses refer to tentative assignments.*

Compound	Solvent	ν_{0-0} (cm.$^{-1}$)	$\nu_{max.}$ (cm.$^{-1}$)	f	$\Delta\nu_{obs.}$ (cm.$^{-1}$)	$\Delta\nu_\pi$ [d] (cm.$^{-1}$)	$\Delta\nu_n$ [e] (cm.$^{-1}$)	$\nu_{H_2O} - \nu_{C_6H_{12}}$ (cm.$^{-1}$)	pK_a
Pyridine	Vap.	34,770			0	0	0		5·23
	C_6H_{12}		37,000 [c]	0·003 [c]					
Pyrimidine	Vap.	31,060	33,790		3710	2300	400		
	C_6H_{12}	30,810	33,500	0·0069	3500			3340	1·30
	H_2O		36,840						
Pyrazine	Vap.	30,870	30,870		3900	4600	−150		
	C_6H_{12}	30,515	30,515	0·0104	6485			2285	0·6
	H_2O		32,800						
Pyridazine	Vap.	(27,390)	30,770		7380	2300	6000		
	C_6H_{12}	(26,790)	29,410	0·0058	7590			3890	2·33 [f]
	H_2O		33,330						
sym-Triazine	Vap.	(31,520)	37,000		3150	2300	400		
	C_6H_{12}	(30,900)	36,750	0·0210	250			1700	—
	H_2O		38,450						
3 : 5 : 6-Trimethyl-1 : 2 : 4-triazine	C_6H_{12}		26,000	0·0079	11,000	5750	6250	2600	2·85
	H_2O		28,600						
m-Tetrazine [a]	Vap.	18,135	18,135		16,635	9200	6500		
	C_6H_{12}	17,880	18,560	0·0042	18,440			1040	<0
	H_2O		19,600						
[b]	C_6H_{12}		31,250	0·001 [c]	5750	(6900)	(−6500)	1530	
	H_2O		32,780						

[a] First $n \longrightarrow \pi$ band. [b] Second $n \longrightarrow \pi$ band. [c] Derived by the method of ref. 6. [d] Calculated by equation (3) with $\Delta\alpha_N = 0{\cdot}6\beta$, and $\beta = 23{,}000$ cm.$^{-1}$. [e] Calculated by equations (5) and (6). [f] Quoted from Albert and Phillips, *J.*, 1956, 1294. [h] Unstable in aqueous solution.

from the case of 3 : 5 : 6-trimethyl-1 : 2 : 4-triazine which, being an alkyl derivative, is not strictly comparable with the unsubstituted azines.

Relative to that of pyridine the $n \longrightarrow \pi$ transitions of the polyazines are displaced to the red region. The displacements are more dependent upon the positions than the number of aza-substituents, *sym*-triazine showing the smallest and 3 : 5 : 6-trimethyl-1 : 2 : 4-triazine the second largest red shift (Table). If the lone-pair orbitals of the azines are assumed to have approximately the same energy, the frequency displacements should

[15] Bayliss and McRae, *J. Phys. Chem.*, 1954, **58**, 1002.

be accounted for by the relative energies of the lowest unoccupied π-orbitals of pyridine and the other azines.

Convenient models for the orbital containing the promoted electron in the excited states of the $n \longrightarrow \pi$ transitions of the azines, covering the series as a whole, are the lowest unoccupied π-orbitals of benzene perturbed by aza-substitution. An alternative description of the $n \longrightarrow \pi$ excited state, the pentadienyl radical and a neutral nitrogen atom, whilst informative in the case of pyridine,[13] is inappropriate for the treatment of the polyazines. The lowest unoccupied π-orbitals of benzene are the degenerate pair, ψ_A and ψ_B, the explicit forms of which are given by

$$\psi_A = (2\phi_1 - \phi_2 - \phi_3 - 2\phi_4 - \phi_5 - \phi_6)/(12)^{\frac{1}{2}} \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$\psi_B = (\phi_2 - \phi_3 + \phi_5 - \phi_6)/2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where the ϕ's are $2p$ atomic orbitals of carbon. On aza-substitution the degeneracy of ψ_A and ψ_B, in general, is removed, the energy of one orbital being lowered more than that

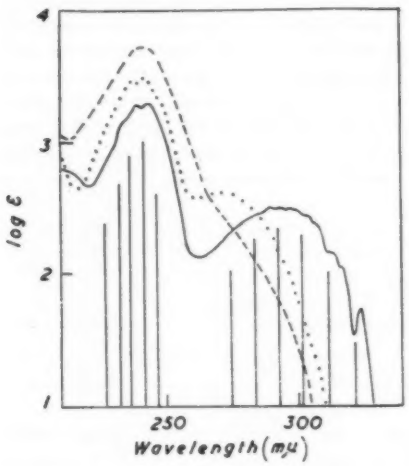


FIG. 1. *The electronic spectrum of pyrimidine:*
———— *in* cyclo*hexane,*
..... *in neutral aqueous solution,*
– – – – *in* 4N-*sulphuric acid* (*spectrum of cation*).
The vertical lines give one of the main progressions in the spectrum of pyrimidine vapour, the heights of the lines representing relative intensities only.

of the other. The forms of the orbitals are qualitatively preserved, however, ψ_B being an exact quantitative representation of the lowest unoccupied level of *sym*-tetrazine (I) and ψ_A giving approximately the form of that of pyrazine (II).

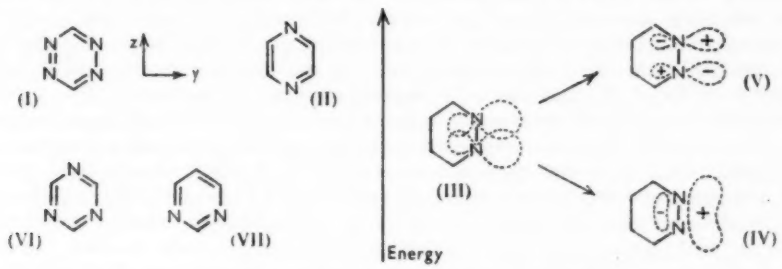
If the relative energies of the $n \longrightarrow \pi$ transitions of the azines are determined primarily by the relative energies of the lowest unoccupied π-orbital, the red shift of the $n \longrightarrow \pi$ bands relative to that of pyridine are given, by first-order perturbation theory, by

$$\Delta\nu_\pi = \nu_{\text{pyridine}} - \nu_{\text{azine}} = [\textstyle\sum_r C_r^2{}_{(\text{azine})} - C_r^2{}_{(\text{pyridine})}]\Delta\alpha_N \quad . \quad . \quad (3)$$

where C_r is the coefficient of a position occupied by a nitrogen in the orbital ψ_A or ψ_B, whichever is lowered the more in energy on aza-substitution, and $\Delta\alpha_N$ is the increment in the Coulomb integral of nitrogen relative to carbon. $\Delta\alpha_N$ being given the empirical value [16] of 0·6β, and β, the carbon–carbon resonance integral, the usual spectroscopic value [17] of 23,000 cm.$^{-1}$, the theoretical red shifts of the $n \longrightarrow \pi$ bands of the azines relative to that of pyridine due to the lowering of the energy of the lowest unoccupied π-orbital are obtained ($\Delta\nu_\pi$). The calculated values ($\Delta\nu_\pi$) do not show good agreement (Table) with the observed red shifts ($\Delta\nu_{obs}$). The discrepancies are particularly large

[16] Mason, *J.*, 1958, 674.
[17] Platt, *J. Chem. Phys.*, 1950, **18**, 1168.

(>5000 cm.$^{-1}$) for the 1 : 2-diaza-compounds, pyridazine, 3 : 5 : 6-trimethyl-1 : 2 : 4-triazine, and *sym*-tetrazine, suggesting that the assumed equality of the energy of the lone-pair orbitals in the azines is untenable. In the 1 : 2-diaza-compounds, lone-pair atomic orbitals are situated on adjacent nitrogen atoms (*e.g.*, III), and these orbitals interact strongly, giving rise to a bonding (*e.g.*, IV) and an antibonding (*e.g.*, V) lone-pair molecular



orbital, both of which are filled with electrons. The lowest energy $n \longrightarrow \pi$ transition in these diaza-compounds is from the antibonding lone-pair molecular orbital, which lies at a higher energy than a lone-pair atomic orbital, so that the $n \longrightarrow \pi$ absorption of these compounds is shifted further to the red region.

The red shift of the $n \longrightarrow \pi$ transitions of the 1 : 2-diaza-compounds due to ground-state interaction can be calculated approximately from the overlap integral of the adjacent lone-pair atomic orbitals. The axes being taken to be those of (I), and trigonal hybridisation being assumed, the lone-pair atomic orbitals (ϕ_{1p}) have the form

$$\phi_{1p} = \phi_s/\sqrt{3} - \phi_{p\sigma}/\sqrt{6} + \phi_{py}/\sqrt{2} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

The overlap integral (S_{1p}) of two such lone-pair orbitals adjacent to one another as in formulæ (I) and (III) is then given by

$$S_{1p} = S_{2s2s}/3 - S_{2s2p\sigma}(2\sqrt{2}/3) + S_{2p\sigma 2p\sigma}/6 + S_{2p\pi 2p\pi}/2 \quad . \quad . \quad . \quad . \quad (5)$$

where $S_{2p\sigma 2p\sigma}$ is the σ overlap integral, and $S_{2p\pi 2p\pi}$ the π overlap integral of two $2p$ orbitals of nitrogen, and S_{2s2s} and $S_{2s2p\sigma}$ are, respectively, the overlap integrals of two $2s$ orbitals and a $2s$ and a $2p$ orbital of nitrogen. The N–N distance in the 1 : 2-diaza-compounds being taken as that found [18] in an *X*-ray diffraction study of *sym*-tetrazine (1·321 Å), and Slater orbitals being used,[19] it is found that the overlap integral of two adjacent lone-pair orbitals is 0·109. The adjacent lone-pair orbital overlap is about one half that of the π-overlap of the $2px$ orbitals of the ring, and it is itself largely of the π-type, the σ contributions to the overlap cancelling one another. The interaction between the adjacent lone-pair atomic orbitals leads to the formation of two lone-pair molecular orbitals with a difference in energy between them (ΔE) given by [20]

$$\Delta E = AS_{1p}I \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

where I is the ionisation potential of an electron in a lone-pair atomic orbital on a nitrogen atom and A is a constant which has the value [20] of 1·16 for σ overlap and 1·53 for π overlap. The ionisation potential of pyridine [21] is 9·23 ev, and though this value may represent the potential required to ionise a π-electron, it is unlikely that the ionisation potential of a lone-pair electron would be greatly different. By equation (6) the energy separation between the lone-pair molecular orbitals of the 1 : 2-diaza-compounds is about 12,000 cm.$^{-1}$, so that the energy of the antibonding orbital lies some 6000 cm.$^{-1}$ above that of a

[18] Bertinotti, Giacomello, and Liquori, *Acta Cryst.*, 1956, **9**, 510.
[19] Mulliken, Rieke, Orloff, and Orloff, *J. Chem. Phys.*, 1949, **17**, 1248.
[20] Mulliken, *ibid.*, 1952, **56**, 295.
[21] Watanabe, *ibid.*, 1957, **26**, 542.

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lone-pair atomic orbital. The $n \longrightarrow \pi$ transitions of the 1 : 2-diaza-compounds are displaced about 6000 cm.$^{-1}$ to the red owing to ground-state interaction, therefore, and this effect, together with the lowering of the benzene-like π-orbitals on aza-substitution, accounts for the observed red shifts of the $n \longrightarrow \pi$ bands of the azines relative to that of pyridine to within about 1500 cm.$^{-1}$.

In the 1 : 3- and 1 : 4-diaza-compounds, ground-state interaction between the lone-pair atomic orbitals is much less important. From the nitrogen–nitrogen distances given by structure determinations of pyrazine [22] and *sym*-triazine,[23] it is found, by the use of Slater orbitals,[19] that the overlap integral between two lone-pair atomic orbitals is 0·004 and 0·009 in the 1 : 4- and the 1 : 3-diaza-compounds, respectively. The overlap is entirely of the σ type in the 1 : 4- and of mixed σ and π types in the 1 : 3-diaza-compounds, the resulting energy difference between the bonding and the antibonding lone-pair molecular orbitals being some 300 cm.$^{-1}$ and about 800 cm.$^{-1}$ in the 1 : 4- and the 1 : 3-diaza-compounds, respectively. Such energies are small, but if 1 : 4- and 1 : 3- as well as 1 : 2-ground-state interaction is considered explicitly, the agreement between the calculated ($\Delta\nu_\pi + \Delta\nu_n$) and the observed ($\Delta\nu_{obs}$) red shifts of the 0–0 bands of the $n \longrightarrow \pi$ transitions of the polyazines, relative to that of pyridine, is brought to within about 1000 cm.$^{-1}$ (Table), apart from the case of the tentatively-assigned second $n \longrightarrow \pi$ transition of *sym*-tetrazine (see below).

In the polyazines the number of lone-pair molecular orbitals equals the number of aza-substituents, but not all transitions from such orbitals to the lowest unoccupied π-orbital are allowed. *sym*-Tetrazine has four lone-pair molecular orbitals, the one of highest energy (ψ_I) having the form

$$\psi_I = (\phi_2 - \phi_3 + \phi_5 - \phi_6)/2 \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

where the ϕ's refer to lone-pair atomic orbitals. ψ_I has the symmetry B_{3g} in D_{2h} (taking axes as in formula I), and it differs in form from the lowest unoccupied π-orbital, ψ_B (symmetry A_u), only in that it possesses no node in the plane of the molecule. An electronic transition from ψ_I to ψ_B is allowed, therefore ($A_g \longrightarrow B_{3u}$), with a transition moment perpendicular to the plane of the molecule. There is no migration of charge from nitrogen to carbon in this transition, the promoted electron being confined to a π-orbital covering only the nitrogen atoms. The transition is quasi-atomic ($2s \longrightarrow 2px$), and there should be no loss of intensity in this transition due to the incomplete overlap of the ground- and excited-state π-electron charge distributions [13]. The remaining three lone-pair molecular orbitals in *sym*-tetrazine have the symmetries, B_{1u}, B_{2u}, and A_g, in descending order of energy, and transitions from them to ψ_B are forbidden. An electronic transition from the most bonding of the lone-pair molecular orbitals of *sym*-tetrazine (symmetry A_g) to the unoccupied π-orbital with the form of ψ_A (symmetry B_{3u}) is allowed, however, and it may be responsible for the second $n \longrightarrow \pi$ band of *sym*-tetrazine, which appears as a shoulder at 3200 Å upon the first $\pi \longrightarrow \pi$ band at 2520 Å in *cyclo*hexane solution (Table; Fig. 2).

In *sym*-triazine (VI) the highest occupied lone-pair molecular orbitals are a degenerate pair (symmetry E' in D_{3h}), and the unoccupied π-orbitals with the forms of ψ_A and ψ_B are also degenerate (symmetry E''). First-order configuration interaction leads to four excited states with the symmetries, A_1'', A_2'', and E'', and of these only the transition to the A_2'' state is allowed, with a transition moment perpendicular to the plane of the molecule. Transitions from the bonding lone-pair molecular orbital (symmetry A_1') to the unoccupied π-orbitals are also forbidden. 1 : 2 : 4-Triazine has the lowest symmetry (C_s) of all the monocyclic azines, and all transitions from the lone-pair molecular orbitals (symmetry A') to the unoccupied π-orbitals (symmetry A'') are allowed.

[22] Wheatley, *Acta Cryst.*, 1957, **10**, 182.
[23] Wheatley, *ibid.*, 1955, **8**, 224; Lancaster and Stoicheff, *Canad. J. Phys.*, 1956, **34**, 1016.

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Pyrazine (II) is unique in the azine series in that ground-state interaction increases the frequency of the $n \longrightarrow \pi$ transition, though the increase is small as 1 : 4-interaction is very weak. Transitions from the higher-energy lone-pair molecular orbital (symmetry B_{1u} in D_{2h} with axes as I) to either of the unoccupied π-orbitals with the forms of ψ_A or ψ_B are forbidden. Only a transition from the bonding lone-pair molecular orbital (symmetry A_g) to the lowest unoccupied π-orbital, ψ_A (symmetry B_{3u}), is allowed. In the cases of pyrimidine (VII) and pyridazine (III) the allowed $n \longrightarrow \pi$ transition is from the higher-energy lone-pair molecular (*e.g.*, V) orbital (symmetry B_2 in C_{2v}) to the lowest unoccupied π-orbital which has the form of ψ_B and the symmetry B_2. The calculated red shifts ($\Delta\nu_\pi + \Delta\nu_n$) of the $n \longrightarrow \pi$ transitions of the polyazines, relative to that of pyridine (Table), refer generally to the allowed transition of lowest frequency, apart from the case of the second $n \longrightarrow \pi$ transition of *sym*-tetrazine.

A subsidiary factor which has influence on the energies and the intensities of the $n \longrightarrow \pi$ transitions of the azines is the percentage "*s*" character of the lone-pair orbitals.

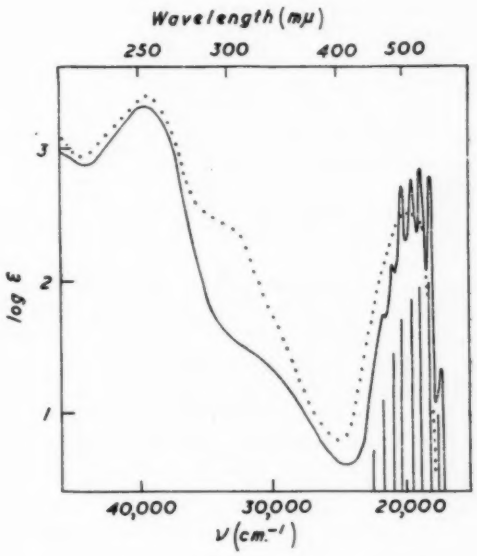

FIG. 2. *The electronic spectrum of* sym-*tetrazine*:

——— *in* cyclo*hexane solution*,
..... *in aqueous solution.*

The vertical lines give the main progression in the visible absorption band of sym-*tetrazine vapour, the heights of the lines representing relative intensities only.*

The CNC and the CNN bond angles of the azines, in the cases where these angles have been determined, suggest that the lone-pair orbitals have somewhat more than trigonal "*s*" character. The CNC angles are 117·5° in pyridine,[24] ~116° in pyrimidine,[25] 115·1° in pyrazine,[22] and 113·2° in *sym*-triazine,[23] whilst in *sym*-tetrazine the CNN angle[18] is 115·95°, indicating that the "*s*" characters of the lone-pair orbitals are 36·8, 38·8, 40·4, 43·6, and 39·0% respectively. Since only the "*s*" component of a *s*–*p* hybrid lone-pair orbital can contribute to the transition moment of a $n \longrightarrow \pi$ absorption, the intensity of the bands should be proportional to the "*s*" character of the lone-pair orbitals. In the series, pyridine, pyrimidine, pyrazine, and *sym*-triazine, the oscillator strength of the $n \longrightarrow \pi$ transition increases with the "*s*" character of the lone-pair orbitals, though the increases are not commensurate with one another (Table). The intensities of the $n \longrightarrow \pi$ bands of the 1 : 2-diaza-compounds are rather low compared with those of the isomeric

[24] Liquori and Viciago, *Ric. sci.*, 1956, **26**, 1848.
[25] Calculated from unpublished crystallographic data for pyrimidine, kindly supplied by Dr. P. J. Wheatley.

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azines, or, in the case of *sym*-tetrazine, relative to the intensity expected from the value of the "*s*" character of the lone-pair orbitals. The low intensity may be due to the strong ground-state interaction in the 1 : 2-diaza-compounds and the spatially forbidden character of $n \longrightarrow \pi$ transitions. In the antibonding lone-pair molecular orbitals (*e.g.*, V) the maxima of the charge distribution are displaced further from the nitrogen nucleus and the π-orbitals than those of the atomic or bonding molecular lone-pair orbitals (*e.g.*, IV), and the displacement may result in a reduced probability of transition.

The percentage "*s*" character of the lone-pair orbitals of the azines may have only a small effect upon the energies of the $n \longrightarrow \pi$ transitions. An electron in a sp^2 orbital of nitrogen has a lower energy than a corresponding p-electron, the ionisation energies of the processes $N(s^2p^3V_3) \longrightarrow N^+(s^2p^2V_2)$ and $N(sp^4V_3) \longrightarrow N^+(sp^3V_2)$ being [26] 13·81 and 14·63 ev, respectively. However, it is probable that orbital-following occurs in the $n \longrightarrow \pi$ transition of an azine, the σ bond orbitals of nitrogen assuming a larger "*s*" character on the promotion of a lone-pair electron to a π-orbital. The stabilisation of the remaining σ electrons due to the increase in their "*s*" character thus partly compensates for that part of the $n \longrightarrow \pi$ transition energy which is required to promote a lone-pair electron from the sp^2 to the p-state. The compensation is likely to be only partial, as the $n \longrightarrow \pi$ transition energies of the azines calculated with neglect of the atomic $sp^2 \longrightarrow p$ promotion term are somewhat low.

In the case of *sym*-tetrazine the $n \longrightarrow \pi$ transition energy can be obtained without the uncertainties arising from the use of perturbation theory and from changes in the Coulomb integral of nitrogen, due to the transfer of charge from nitrogen to carbon in the transition. The lowest unoccupied π-orbital of *sym*-tetrazine is ψ_B (eqn. 2), which lies at an energy of β_{NN} above that of a $2p$ atomic orbital of nitrogen. The highest occupied lone-pair molecular orbital is ψ_I (eqn. 7), which lies at an energy of about 6500 cm.$^{-1}$ above that of an atomic sp^2 hybrid orbital of nitrogen (Table). By giving the nitrogen–nitrogen resonance integral, β_{NN}, the same value as the carbon–carbon resonance integral [17] (23,000 cm.$^{-1}$), and by neglecting the atomic $sp^2 \longrightarrow p$ promotion term, the calculated $n \longrightarrow \pi$ transition energy is found to be 16,500 cm.$^{-1}$ for *sym*-tetrazine, compared with the experimental value of 18,000 cm.$^{-1}$ (Table). The $n \longrightarrow \pi$ transition energies of the other unsubstituted azines, calculated with neglect of the atomic $sp^2 \longrightarrow p$ promotion energy, are similarly 1500—3400 cm.$^{-1}$ lower than the observed values. If the deficits are due to the neglected energy term, orbital-following in a $n \longrightarrow \pi$ transition is likely, since from ionisation data [26] the atomic $sp^2 \longrightarrow p$ promotion energy is 6600 cm.$^{-1}$ for nitrogen.

Experimental

Materials.—Pyrimidine was kindly supplied by Dr. N. Whittaker,[27] 3 : 5 : 6-trimethyl-1 : 2 : 4-triazine by Dr. R. Metze,[28] and *sym*-triazine by Dr. C. Grundmann.[29] *sym*-Tetrazine was prepared by the method of Curtius, Darapsky, and Müller,[1] and the remaining compounds were commercial specimens.

Absorption Spectra.—In the vapour and in *cyclo*hexane the spectra of the monocyclic azines were measured with a Cary recording spectrophotometer; the spectra in aqueous solution were measured, and those in *cyclo*hexane checked, with Hilger Uvispek quartz spectrophotometers.

The author thanks Dr. P. J. Wheatley for unpublished data on the structure of pyrimidine, the Australian National University for a Research Fellowship, University College, London, for the provision of facilities, and the Royal Society for the loan of a spectrophotometer.

Chemistry Department, The University, Exeter. [*Received, July 29th*, 1958.]

[26] Mulliken, *J. Chem. Phys.*, 1934, **2**, 782.
[27] Whittaker, *J.*, 1953, 1646.
[28] Metze, *Ber.*, 1955, **88**, 772.
[29] Grundmann and Kreutzberger, *J. Amer. Chem. Soc.*, 1954, **76**, 632.

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246. *The Electronic Spectra of N-Heteroaromatic Systems. Part II.* Substituted Monocyclic Azones.*

By S. F. Mason.

The visible and ultraviolet absorption spectra of the monocyclic azines and some derivatives have been measured in polar and non-polar solvents. The $n \longrightarrow \pi$ bands of the azines are shifted towards the blue region by electron-donating and towards the red region by electron-accepting substituents, whilst the $\pi \longrightarrow \pi$ bands undergo bathochromic shifts with both types of substituent. The shift of the $n \longrightarrow \pi$ band of an azine on substitution is shown to be due primarily to the effect of the substituent on the energy of the lowest unoccupied benzene-like π-orbital of the azine.

The absorption bands due to $\pi \longrightarrow \pi$ transitions in the electronic spectrum of benzene and the monocyclic azines, in general, are shifted towards the red region by both electron-donating and electron-accepting substituents, as either group reduces the energy separation between the highest occupied and the lowest unoccupied π-orbital. In the spectra of the monocyclic azines, however, the absorption band due to the transition of an electron from a lone-pair orbital to a π-orbital of the ring is shifted towards the blue region by *ortho–para*-directing substituents, notably, the halogens and the methyl group, which have been the main substituents hitherto studied.[1-4] The effects of two *meta*-directing substituents (nitrile and carboxyl) and a more powerful *ortho* : *para*-directing substituent (methoxyl) upon the positions of the $n \longrightarrow \pi$ bands of the monocyclic azines have now been investigated. The visible and ultraviolet absorption spectra of the monocyclic azines and their derivatives have been measured in *cyclo*hexane, ethanol, and aqueous solution, the results being recorded in the Table and the Figs.

The band of longest wavelength in the spectra of the azines and their derivatives is relatively weak ($\varepsilon_{max.} \simeq 200$—$1000$), and it shows a pronounced blue shift on change from *cyclo*hexane to aqueous solution (Table; Fig. 1). These features suggest that the band is due to the transition of a non-bonding electron from a lone-pair orbital of a nitrogen atom to a π-orbital of the ring.[5-8] The low intensity of the band arises because the lone-pair and the π-orbitals of an azine are concentrated in different regions of space,[5] and because only the *s*-component of the *s–p* hybrid lone-pair orbital can contribute to the transition moment of a $n \longrightarrow \pi$ excitation.[8] The blue shifts of the $n \longrightarrow \pi$ bands in the electronic spectra of the azines observed on changing from *cyclo*hexane to aqueous solution are due[6,7] to the stabilisation of the ground state by hydrogen-bonding in the water, an increase in the transition energy being required to break or weaken the hydrogen bonds. In aqueous solution sufficiently acid to form the cation of the azine, the $n \longrightarrow \pi$ bands undergo further blue shifts or disappear (Table; Fig. 1), as the lone-pair electrons either bind a proton or are held more strongly in their orbital by inductive and inductomeric effects originating from a charged centre elsewhere in the cation.

In contrast to the $\pi \longrightarrow \pi$ bands of the azines, which undergo bathochromic shifts generally upon substitution, the $n \longrightarrow \pi$ bands, for the most part, move towards the blue region with *ortho–para*-directing substituents and towards the red region with *meta*-directing groups (Table; Figs. 1—3). The direction and the magnitudes of the shifts are not always apparent from the wavelength of maximum absorption, particularly for

* Part I, preceding paper.

[1] Uber and Winters, *J. Amer. Chem. Soc.*, 1941, **63**, 137.
[2] Rush and Sponer, *J. Chem. Phys.*, 1952, **20**, 1847.
[3] Halverson and Hirt, *ibid.*, 1951, **19**, 711.
[4] Stephenson, *ibid.*, 1954, **22**, 1077.
[5] Platt, *ibid.*, 1951, **19**, 101.
[6] Kasha, *Discuss. Faraday Soc.*, 1950, **9**, 14.
[7] McConnell, *J. Chem. Phys.*, 1952, **20**, 700.
[8] Orgel, *J.*, 1955, 121.

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pyrazine (I) and its derivatives in *cyclo*hexane. The 0–0 vibrational peak of the $n \longrightarrow \pi$ band of pyrazine in *cyclo*hexane has the maximum intensity, but in 2-methylpyrazine the 0–1 and in 2 : 5-dimethylpyrazine the 0–2 vibrational peak is the most intense, whilst in dimethyl pyrazine-2 : 3-dicarboxylate the vibrational fine structure of the $n \longrightarrow \pi$ band is completely blurred (Fig. 1). Thus, this ester absorbs at longer wavelengths than pyrazine (Fig. 1), though the $\lambda_{max.}$ of the $n \longrightarrow \pi$ band lies at a shorter wavelength (Table). A similar effect occurs in the case of pyrimidine (II) and its 2-methoxycarbonyl derivative in *cyclo*hexane (Table). In polar solvents the wavelengths of maximum absorption give more accurately the shifts of the $n \longrightarrow \pi$ bands due to substitution, as the vibrational

FIG. 1. *The ultraviolet absorption spectra of pyrazine —— in* cyclo*hexane and — · — · — in* 5N*-sulphuric acid, and the spectra in* cyclo*hexane of — — — — 2 : 5-dimethylpyrazine and . . . . . dimethyl pyrazine-2 : 4-dicarboxylate.*

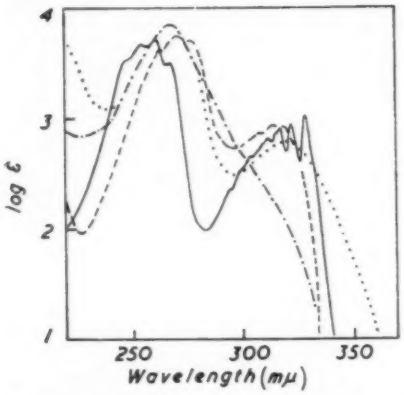
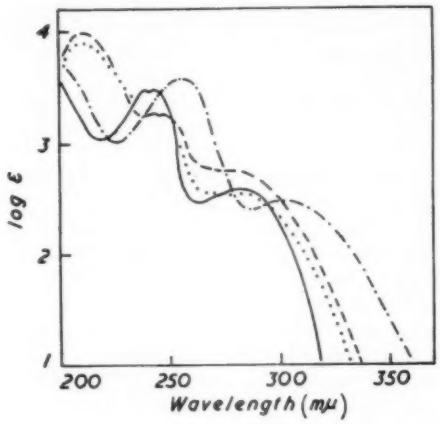
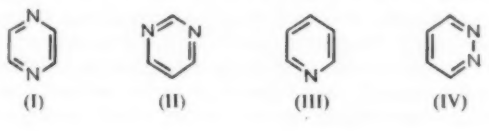


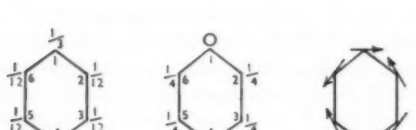
FIG. 2. *The ultraviolet absorption spectra in ethanol of —— pyrimidine and of . . . . . pyrimidine-2-, — · — · — -4-, and — — — -5-carboxylic acid.*



fine structure of the $n \longrightarrow \pi$ bands of the azines and their derivatives is completely blurred in these solvents (Fig. 2). However, pyrimidine-2-carboxylic acid absorbs at longer wavelengths than does pyrimidine in ethanol (Fig. 2), though the $\lambda_{max.}$ of the $n \longrightarrow \pi$ band lies at a slightly shorter wavelength (Table).

The shifts observed on substitution support further the assignment of the low-intensity long-wavelength bands of the azines to the transition of an electron from a lone-pair





orbital of a nitrogen atom to a π-orbital of the ring. In general, electronic charge is transferred from nitrogen to carbon in the excited state of such a transition, and, relative to the ground state, the excited state is stabilised by electron-accepting and destabilised

by electron-donating substituents, the former reducing and the latter increasing the transition energy.

In the less symmetrical azines the shift of the $n \longrightarrow \pi$ band produced by a given group varies markedly with the position of substitution. In pyrimidine a 4-methoxy- produces a larger blue shift than a 2-methoxy-group (Table), and a carboxyl group at position 4 gives a larger red shift than one at the 2- or the 5-position (Fig. 2). Similarly, in pyridine (III) and pyridazine (IV) a given substituent gives rise to larger shifts of the $n \longrightarrow \pi$ band, towards the red or the blue region depending upon the electron-accepting or -donating property of the group, when in the 4-position than when elsewhere in these rings (Table; Fig. 3).

The relative magnitudes of the shifts produced by a given group substituted at different positions in an azine appear to be governed largely by the change in the energy of the excited state of the $n \longrightarrow \pi$ transition on substitution. Suitable models for the orbital containing the promoted electron in the excited states of the $n \longrightarrow \pi$ transitions of the azines are the lowest unoccupied π-orbitals of benzene, perturbed by aza-substitution.[9]

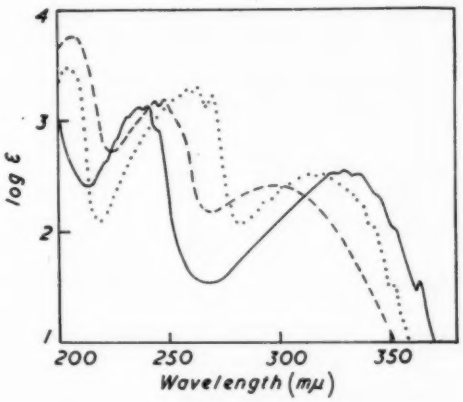


FIG. 3. *The ultraviolet spectra in* cyclohexane *of* —— *pyridazine and of* . . . . 3-, *and* — — — 4-*methoxypyridazine.*

The lowest unoccupied π-orbitals of benzene are the degenerate pair, ψ_A and ψ_B, defined in Part I; the charge distributions in ψ_A and ψ_B are given in (V) and (VI), respectively. On aza-substitution the degeneracy of ψ_A and ψ_B, in general, is removed, the energy of one orbital being lowered more than that of the other, though the forms of the orbitals, notably the charge distributions, are qualitatively preserved.

In pyridine (III) and pyrazine (I) ψ_A becomes the lowest unoccupied π-orbital, the nitrogen atoms being substituted at the 1- and the 1 : 4-positions of (V), respectively. In pyridine a non-bonding electron on promotion from the lone-pair orbital assumes a distribution given approximately by (V) in the excited state, so that $C_{(4)}$ receives the largest share of the charge transferred from the nitrogen atom. A substituent should have a greater effect upon the position of the $n \longrightarrow \pi$ band of pyridine when in the 4- than when in the 2- or 3-position, as is observed in the case of the electron-accepting nitrile group which causes red shifts in the order, 4- $>$ 3- $\geqslant$ 2-position (Table). The near equality of the red shifts in the $n \longrightarrow \pi$ band of pyridine produced by the nitrile group in the 2- and the 3-position, and the equality of the charges at those positions in (V), is probably accidental. At a higher level of approximation it can be shown [8] that more charge is transferred to the 2- than to the 3-position in the $n \longrightarrow \pi$ transition of pyridine, so that the excited state should be more stabilised by the 2- than the 3-nitrile group. However, this effect is compensated by the tighter binding of the lone-pair electrons in the ground

[9] Preceding paper.

state of 2- than of 3-cyanopyridine, owing to the inductive effect, as shown by the ionisation constants of these compounds (Table). In pyrazine each carbon atom receives the same amount of charge from the nitrogen atoms in the excited state of the $n \longrightarrow \pi$ transition, in conformity with the observation [3] that the $n \longrightarrow \pi$ band of pyrazine moves towards the blue region with nearly equal energy increments as the hydrogen atoms are successively replaced by chlorine.

In pyridazine (IV) and pyrimidine (II) ψ_B becomes the lowest unoccupied π-orbital, with the nitrogen atoms at the 2 : 3- and the 2 : 5-positions of (VI), respectively. The nodal axis through the 1 : 4-positions of (VI) is preserved in the lowest unoccupied π-orbital of pyrimidine, as it coincides with the C_2 axis of this azine. In the excited state of the $n \longrightarrow \pi$ transition of pyrimidine, therefore, charge is transferred from the nitrogen atoms only to the carbon atoms at the 4- and the 6-position. A substituent in the 2- or the 5-position of pyrimidine should not change the energy of the excited state of the $n \longrightarrow \pi$ transition, whilst in the 4-position the effect of a substituent should be large. The powerful electron-donating methoxyl group produces only a small blue shift in the $n \longrightarrow \pi$ band of pyrimidine when in the 2-position but a large shift when in the 4-position (Table). Similarly the electron-attracting carboxyl group gives a small red shift in the 2- or the 5-position of pyrimidine and a large bathochromic shift when in the 4-position (Fig. 2).

The visible and ultraviolet absorption spectra of the monocyclic azines and their derivatives in polar and non-polar solvents. Values in italics refer to shoulders or inflexions.

Compound	pK_a	Solvent	$n \longrightarrow \pi$ bands $\lambda_{max.}$ (mμ)	$\varepsilon_{max.}$	$\pi \longrightarrow \pi$ bands $\lambda_{max.}$ (mμ)	$\varepsilon_{max.}$
Pyridine	5·23 [a]	C_6H_{12}	*270* [c]	*450* [c]	251	2000
		pH 0	[b]	[b]	257	2650
2-Cyano-	−0·26 ± 0·04	C_6H_{12}	*278* [c]	*340* [c]	265	2730
		pH 7	[b]	[b]	265	3790
		10N-H_2SO_4	[b]	[b]	267	7520
3-Cyano-	1·36 ± 0·03	C_6H_{12}	*279* [c]	*430* [c]	265	2230
		pH 7	[b]	[b]	265	2890
		4N-H_2SO_4	[b]	[b]	265	5130
4-Cyano-	1·90 ± 0·02	C_6H_{12}	*290*	*500* [c]	271	2840
		pH 7	[b]	[b]	275	3410
		2N-H_2SO_4	[b]	[b]	276	5710
2 : 6-Dicyano-	< −2·0	C_6H_{12}	[b]	[b]	275	3990
		pH 7	[b]	[b]	274	4900
Pyrazine	0·6 [a]	C_6H_{12}	328	1040	260	5600
		EtOH	310	860	261	6000
		pH 7	300	850	261	5900
		5N-H_2SO_4	[b]	[b]	266	7300
2-Methyl-	1·47 ± 0·04	C_6H_{12}	320	830	266	5700
		pH 7	*295*	*1120*	271	5910
		2N-H_2SO_4	[b]	[b]	276	6680
2 : 5-Dimethyl-	1·97 ± 0·02	C_6H_{12}	314	908	271	5700
		pH 7	*295*	*2000*	276	6840
		2N-H_2SO_4	[b]	[b]	285	8080
2 : 3-Dimethoxycarbonyl-	< −2·0	C_6H_{12}	319	660	268	6820
		EtOH	311	700	268	6950
		pH 7	303	740	268	7100
2 : 3-Dicarboxy-	3·57 ± 0·02	EtOH	314	690	269	6200
	0·9 ± 0·2	pH 7	*315*	*970*	281	7820
	< −2·0	pH 2·2	*305*	*812*	274	6440
		5N-H_2SO_4	*310*	*708*	270	6940
2-Methoxy-	0·75 [a]	C_6H_{12}	[b]	[b]	277	5760
		pH 7	[b]	[b]	290	5240
Pyridazine	2·33 [a]	C_6H_{12}	340	315	246	1300
		EtOH	313	303	246	1160
		pH 7	300	320	247	1090
		pH 0	[b]	[b]	238	1610
3-Methyl-		EtOH	310 [d]	400 [d]	251 [d]	1300 [d]
4-Methyl-	2·92 ± 0·01	C_6H_{12}	331	375	252	1296
		EtOH	303 [d]	350 [d]	250 [d]	1370 [d]
		pH 7	292	371	247	1440
		pH 0·7	[b]	[b]	221	6020

TABLE. (*Continued.*)

Compound	pK_a	Solvent	$n \longrightarrow \pi$ bands $\lambda_{max.}$ (mμ)	$\varepsilon_{max.}$	$\pi \longrightarrow \pi$ bands $\lambda_{max.}$ (mμ)	$\varepsilon_{max.}$
3-Methoxy-	2·52 [a]	C_6H_{12}	327	326	272	1990
		pH 7	*300*	*329*	265	2330
		pH 0·5	[b]	[b]	269	2010
4-Methoxy-	3·70 [a]	C_6H_{12}	307	258	259	1560
		pH 7	*285*	*390*	254	2570
		pH 1	[b]	[b]	247	10,320
3 : 6-Dimethoxy-		C_6H_{12}	*325*	*312*	292	2500
		pH 7	[b]	[b]	284	2270
4 : 5-Dicarboxy-	3·30 ± 0·02	EtOH	345	274	266	3020
		pH 7	313	337	253	3520
		pH 1	*325*	*364*	263	3330
Pyrimidine	1·30 [a]	$C_{6\ 12}$	298	326	243	2030
		EtOH	280	373	243	2920
		pH 7	271	422	243	3210
		4N-H_2SO_4	[b]	[b]	242	5540
2-Methoxy-	<1 [a]	C_6H_{12}	*295*	*400*	264	4180
		pH 7	[b]	[b]	267	4530
4-Methoxy-	2·5 [a]	C_6H_{12}	*270*	*274*	248	3100
		pH 7	[b]	[b]	248	3370
5-Hydroxy-		EtOH	[b]	[b]	276	5330
2-Methoxycarbonyl-	−0·68 ± 0·04	C_6H_{12}	290	370	247	1840
		pH 7	*270*	*382*	245	2300
		12N-H_2SO_4	[b]	[b]	247	4900
2-Carboxy-	2·85 ± 0·02	EtOH	277	374	246	2120
	−1·13 ± 0·05	pH 7	*275*	*410*	246	2620
		pH 0·8	*270*	*441*	240	2690
4-Carboxy-		EtOH	303	295	256	3820
5-Carboxy-		EtOH	*280*	*561*	247	1870
3 : 5 : 6-Trimethyl-1 : 2 : 4-triazine	2·85 ± 0·02	C_6H_{12}	384	520	264	5100
		pH 7	350	440	263	4700
		pH 0	[b]	[b]	245	4400
3-Amino-1 : 2 : 4-triazine	4·00 ± 0·02	C_6H_{12}	394	505	310	2730
		pH 7	*350*	*1100*	319	2820
sym-Tetrazine	<0	C_6H_{12}	542	829	252	2150
			320	*26*		
		pH 7	510	362	255	2840
			305	*157*		
1 : 4-Dimethyl-		C_6H_{12}	562	832	273	3720
		pH 7	519	365	276	3800
1 : 4-Dicarboxy-	2·8 ± 0·2	pH 7	515	202	251	3100

[a] Quoted from Albert and Phillips, *J.*, 1956, 1294. [b] The $n \longrightarrow \pi$ band is absent or not measurable. [c] Derived by the method of ref. 4. [d] Quoted from Eichenberger, Rometsch, and Druey, *Helv. Chim. Acta*, 1954, **37**, 1298.

Pyrimidine-5-carboxylic acid absorbs at slightly longer wavelengths than the 2-isomer (Fig. 2), suggesting that in the latter the lone-pair electrons of the nitrogen atoms are bound more firmly in the ground state by the inductive effect of the substituent. However, the spectra of the pyrimidine-carboxylic acids illustrate that, in general, the position of the $n \longrightarrow \pi$ band in a substituted azine, relative to that of the parent compound, is determined primarily by the effect of the substituent upon the energy of the excited state.

The nodal axis through the 1 : 4-positions of (VI) is not preserved in the lowest unoccupied orbital of pyridazine (IV), as the C_2 axis of the molecule bisects bonds and does not run through atomic positions. Thus, a small amount of charge is transferred from the nitrogen atoms to the carbon atoms at positions 3 and 6 of pyridazine (IV) in the excited state of the $n \longrightarrow \pi$ transition, though the major transfer of charge takes place to those at positions 4 and 5. Accordingly, a given substituent in the 2-position of pyrimidine and the 3-position of pyridazine should produce a somewhat larger shift of the $n \longrightarrow \pi$ band of the azine in the latter case, whilst in the 4-positions of these azines the substituent should give rise to much larger shifts, which should be comparable with one another. It is found (Table; Fig. 3) that the methoxyl group produces red shifts of 3

and 28 mμ in the 2- and the 4-positions of pyrimidine, respectively, and of 13 and 33 mμ in the 3- and the 4-positions of pyridazine, respectively.

Less information is available on the effect of substituents on the position of the $n \longrightarrow \pi$ band of the polyazines. Chloro- and methyl groups produce the expected blue shift in the $n \longrightarrow \pi$ band of *sym*-triazine,[10] but the methyl group moves the $n \longrightarrow \pi$ band of *sym*-tetrazine towards the red region (Table). The lowest unoccupied π-orbital in *sym*-tetrazine is of the form of ψ_B, the charge distribution being confined to the nitrogen atoms. No charge is transferred from nitrogen to carbon in the $n \longrightarrow \pi$ transition of *sym*-tetrazine, and the energy of the excited state should not be changed by substituents. The red shifts produced by methyl and carboxyl groups may be due to a modification, consequent upon substitution, of the ground-state interaction between the four lone-pair orbitals.[9]

Some features of the first $\pi \longrightarrow \pi$ band of the substituted azines may be accounted for qualitatively by the theory of Sklar,[11] Forster,[12] Platt,[13] and Murrell and Longuet-Higgins,[14] on the assumption that this band corresponds to the 260 mμ band of benzene perturbed by the ring nitrogen and the exocyclic substituents. The intensity changes in the 260 mμ band of benzene, following substitution, can be derived [11-13] by adding vectorially, according to the scheme of (VII), migration moments [11] or spectroscopic moments [13] characteristic of the substituents. The wavelength shift of the band on the poly-substitution of benzene may be obtained [12] from the intensity increment and an additional parameter. The spectroscopic moments [13] of the substituents studied in the present work are: OH 23, OMe 31, Me 7, CN −19, CO_2H −28, and aza-N −38.

The intensity of the first $\pi \longrightarrow \pi$ band of the unsubstituted azines is explained only qualitatively by the appropriate vector addition of the spectroscopic moment of the ring-nitrogen atom according to (VII). Quantitatively the intensities of the first $\pi \longrightarrow \pi$ band in pyrimidine and pyridazine, and in pyrazine and *sym*-tetrazine, should be equal, but the 1 : 2-diaza-compound of each pair absorbs with the lower intensity (Table). Qualitatively, however, the intensity and wavelength changes follow the order expected in both the azines and their derivatives. In the 2- and the 3-position of pyridine the nitrile group produces smaller increases in the wavelength and the intensity of maximum absorption than when it is in the 4-position (Table). The intensity of the $\pi \longrightarrow \pi$ band of pyrimidine is reduced and moved very little towards the red region by a carboxyl group at position 2 or 5, but at the 4-position the group enhances the intensity and gives a large red shift (Fig. 2). Conversely a hydroxyl or methoxyl group in the 2- or the 5-position of pyrimidine gives rise to a large bathochromic shift and intensity increase, but with a methoxyl group at position 4 such changes are small (Table). Similarly, the effects of substituents upon the position and the intensity of the $\pi \longrightarrow \pi$ band of pyridazine are qualitatively those expected from the signs and the magnitudes of the spectroscopic moments of the substituents, but in pyrazine- and *sym*-tetrazine-dicarboxylic acids the expected diminution in the intensity of the $\pi \longrightarrow \pi$ band is not observed (Table).

Experimental

Absorption Spectra.—These were measured with Hilger Uvispek Quartz Spectrophotometers, the solvents listed in the Table being used.

Ionisation Constants.—These were determined by potentiometric titration of 0·1—0·01M-solutions, a Cambridge pH meter being used with glass and calomel electrodes for compounds with pK_a values >1. pK_a values <1 were determined spectrophotometrically at 0·0001M.

Materials.—The unsubstituted azines were as in Part I.[9] 5-Hydroxypyrimidine and pyrimidine-4- and -5-carboxylic acid were kindly provided by Dr. J. F. W. McOmie,[15] pyrimidine-

[10] Hirt, Halverson, and Schmitt, *J. Chem. Phys.*, 1954, **22**, 1148.
[11] Sklar, *ibid.*, 1942, **10**, 135.
[12] Forster, *Z. Naturforsch.*, 1947, **2a**, 149.
[13] Platt, *J. Chem. Phys.*, 1951, **19**, 263.
[14] Murrell and Longuet-Higgins, *Proc. Phys. Soc.*, 1955, **68**, *A*, 329.
[15] Boarland and McOmie, *J.*, 1952, 3716.

2-carboxylic acid and its methyl ester by Dr. A Holland,[16] 4-methyl-, 3- and 4-methoxy-, and 3 : 6-dimethoxy-pyridazine by Dr. K. Eichenberger and Dr. J. Druey,[17] and 3 : 5 : 6-trimethyl-1 : 2 : 4-triazine by Dr. R. Metze.[18] Pyrazine-2 : 3-dicarboxylic acid and its dimethyl ester were prepared by Gabriel and Sonn's method,[19] and pyridazine-4 : 5-dicarboxylic acid by Gabriel's method.[20] 1 : 4-Dimethyltetrazine and tetrazine-1 : 4-dicarboxylic acid were prepared by the methods of Curtius, Darapsky, and Müller,[21] and 3-amino-1 : 2 : 4-triazine by Erickson's method.[22]

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CHEMISTRY DEPARTMENT, THE UNIVERSITY, EXETER. [*Received, August 7th*, 1958.]

[16] Holland, *Chem. and Ind.*, 1954, 786.
[17] Eichenberger, Rometsch, and Druey, *Helv. Chim. Acta*, 1954, **37**, 1298; Staehelin, Eichenberger, and Druey, *ibid.*, 1956, **39**, 1741.
[18] Metze, *Ber.*, 1955, **88**, 772.
[19] Gabriel and Sonn, *Ber.*, 1907, **40**, 4850.
[20] Gabriel, *Ber.*, 1903, **36**, 3373.
[21] Curtius, Darapsky, and Müller, *Ber.*, 1907, **40**, 84; 1915, **48**, 1614.
[22] Erickson, *J. Amer. Chem. Soc.*, 1952, **74**, 4706.

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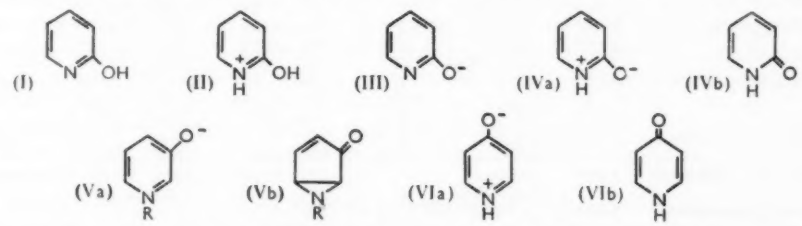
247. *The Electronic Spectra of N-Heteroaromatic Systems. Part III.* The $\pi \rightarrow \pi$ Transitions of the Monocyclic Hydroxy-azines.*

By S. F. MASON

The ultraviolet absorption spectra of the enolic, cationic, anionic, and zwitterionic forms of the monocyclic hydroxy-azines have been measured in aqueous solution, and the spectra of the enols and zwitterions, fixed as the *O*- and the *N*-methyl derivatives, respectively, have been obtained in non-polar solvents. The first absorption band in the spectra of the different charged forms of a given compound lie at wavelengths in the sequence, zwitterion > anion > cation > enol, and the spectrum of the zwitterion shifts considerably towards the red region on changing from aqueous to non-polar solvents. The solvent effect is inconsistent with the valence-bond theory of the spectra, and a molecular-orbital theory is developed to account for the solvent shifts and the spectral differences between the compounds studied and their various charged forms.

THE hydroxy-derivatives of *N*-heteroaromatic systems can exist, in general, as any one of four different species, the neutral enol (*e.g.* I), the cation (*e.g.* II), the anion (*e.g.* III), and the zwitterion (*e.g.* IVa) or amide (*e.g.* IVb). In *N*-heteroaromatic hydroxy-compounds,



the zwitterionic or amide form of a given compound usually absorbed [1] radiation at longer wavelengths than the enol, use being made of this property to determine the concentration

* Part II, preceding paper.
[1] Mason, *J.*, 1957, 5010.

TABLE. 1. *The electronic absorption spectra of the enol (E), cation (C), anion (A), and zwitterion (Z) of some N-heteroaromatic hydroxy-compounds and their O- and N-methyl derivatives. The oscillator strength (f) of the* $\pi \longrightarrow \pi$ *absorption band of longest wavelength in the spectra of the enolic and zwitterionic forms. Values in italics refer to shoulders.*

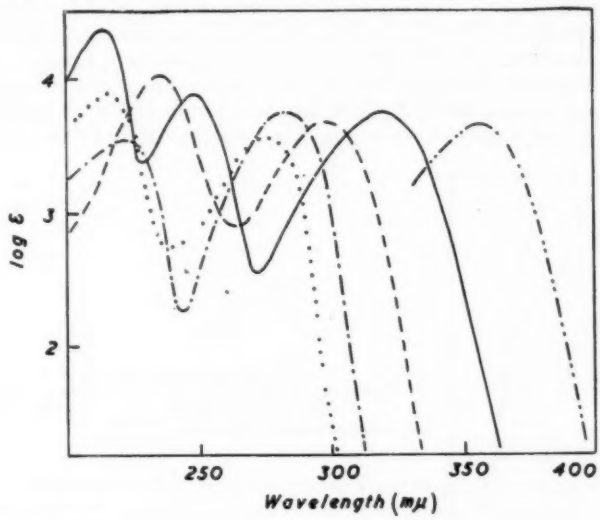
Compound	pK_a	Solvent	Species	$\lambda_{max.}$ (mμ)	$\varepsilon_{max.}$	*f*
2-Hydroxypyridine	0·75 [a]	pH 6	Z	293; *224* [a]	5890; 7230 [a]	0·117
	11·62 [a]	pH 13	A	291; 230	5070; 9000	
		10N-H_2SO_4	C	277; 209	6950; 3600	
2-Methoxypyridine	3·28 [a]	pH 7	E	269; <205 [a]	3230; >5300	0·065
		pH 1	C	279; 210	6920; 3550	
1-Methyl-2-pyridone	0·32 [a]	pH 5	Z	297; 226 [a]	5700; 6100 [a]	0·110
		10N-H_2SO_4	C	279; 210	6250; 3500	
3-Hydroxypyridine	4·86 [a]	pH 6·8	Z + E	315; 278; 246 [a]	3060; 2320; 5120 [a]	—
	8·72 [a]	pH 13	A	298; 236	4960; 11,000	
		pH 2	C	283; 222	5840; 3730	
3-Methoxypyridine	4·88 [a]	pH 7	E	276; 216 [a]	3960; 8320 [a]	0·052
		pH 2	C	284; 224	6240; 4290	
3-Hydroxypyridine 1-methochloride	4·96 [a]	pH 7	Z	320; 249 [a]	5810; 8120	0·088
		pH 2	C	288; 224	5900; 3790	
4-Hydroxypyridine	3·27 [a]	pH 7	Z	253	14,800	0·296
	11·09 [a]	pH 13	A	*260*; 239	*2200*; 14,150	
		pH 0	C	234	9800	
4-Methoxypyridine	6·62 [a]	pH 9	E	*235*; 222	*2000*; 9300	~0·05
		pH 4	C	235	9500	
1-Methyl-4-pyridone	3·33 [a]	pH 7	Z	260	18,900	0·328
		pH 1	C	239	11,800	
2-Hydroxypyrazine	−0·1 [a]	pH 5	Z	317; 221	5520; 8820	0·128
	8·23 [a]	pH 10·5	A	316; 227	5640; 11,240	
		10N-H_2SO_4	C	342; 222	6220; 10,400	
2-Methoxypyrazine	0·75 [a]	C_6H_{12} [d]	E	277; 210	5760; 11,500	—
		pH 7	E	290; 209 [a]	5240; 9600 [a]	0·108
		5N-H_2SO_4	C	304; 218	6900; 9220	
1-Methyl-2-pyrazone	−0·04 [a]	pH 7	Z	321; 224 [a]	5830; 9100 [a]	0·129
		10N-H_2SO_4	C	345; 225	6410; 10,900	
3-Hydroxypyridazine	−1·8 [a]	pH 6	Z	281; 220 [a]	2790; 3160 [a]	0·069
	10·46 [a]	pH 13	A	295; 227	2850; 5910	
		15N-H_2SO_4	C	265; 215	2560; 2750	
3-Methoxypyridazine	2·52 [a]	pH 6	E	265; <210	2330; >3000	0·058
		C_6H_{12} [d]	E	272; 214	1990; 3140	
		pH 0	C	269; 217	2010; 2490	
4-Hydroxypyridazine	1·07 [a]	pH 4·8	Z	262 [a]	12,740 [a]	0·287
	8·68 [a]	pH 13	A	270; 245	4650; 12,840	
		5N-H_2SO_4	C	244	8400	
4-Methoxypyridazine	3·70 [a]	pH 7	E	254; 224 [a]	2570; 8240	0·06
		C_6H_{12} [d]	E	259; 216	1560; 5970	
		pH 1	C	247	10,320	
2-Hydroxypyrimidine	2·24 [b]	pH 6·0	Z	298; 212	4750; 10,820	0·091
	9·17 [b]	pH 13	A	292; 220	4600; 11,700	
		pH 0	C	309; <210	5700; >10,000	
2-Methoxypyrimidine	~1	pH 7	E	264; <210	4660; >6000	0·072
		C_6H_{12} [d]	E	264; <210	4180; >7500	
		5N-H_2SO_4	C	273; <210	5020; >9000	
4-Hydroxypyrimidine	1·69 [b]	pH 6·2	Z	*260*; 223 [b]	*3740*; 7320 [b]	~0·09
	8·60 [b]	pH 13	A	263; 227 [b]	3280; 11,100 [b]	
		5N-H_2SO_4	C	251; 224 [b]	2970; 9840 [b]	
4-Methoxypyrimidine	2·5 [b]	pH 7	E	248; <215	3370; >6500	0·066
		C_6H_{12} [d]	E	248; <215	3100; >6000	
		pH 0	C	*240*; 227	6700; 7750	
1-Methyl-4-pyrimidone	2·02 [c]	pH 6	Z	240	14,600	0·315
		pH 0	C	*250*; 229	*2650*; 10,200	
3-Methyl-4-pyrimidone	1·84 [b]	pH 5	Z	269; 221 [b]	3900; 6810 [b]	0·095
		2·5N-HCl	C	258; 226 [b]	2940; 9080 [b]	
5-Hydroxypyrimidine	1·87 [c]	pH 4·32	Z + E	*325*; 271; 214 [a]	*107*; 4750; 9720 [a]	—
	6·78 [b]	pH 9·5	A	304; 238	4450; 11,240	
		2N-H_2SO_4	C	285; 223	4700; 6950	
		EtOH	E	276; 218 [a]	5330; 9970 [a]	0·098

[a] Quoted from ref. 3. [b] Quoted from ref. 5. [c] Quoted from ref. 4. [d] *cyclo*Hexane solution; only the $\pi \longrightarrow \pi$ bands are listed. [e] Quoted from ref. 1.

of the tautomers at equilibrium.[1] To study further the effect of ionisation on the light absorption of these compounds, the ultraviolet spectra of the anionic and cationic species of a number of *N*-heteroaromatic hydroxy-compounds have now been measured in aqueous solution, and, to throw light on the nature of the electronic transitions involved, the effect of change of solvent upon the spectra of the enolic and zwitterionic forms, fixed as the *O*- and *N*-methyl derivative of the compounds, respectively, has been investigated. The results obtained are recorded in the Tables and the Figures.

In general, it is found (Table 1; Figs. 1 and 2) that the long-wave absorption bands in the spectra of the different charged species of a given *N*-heteroaromatic hydroxy-compound lie at wavelengths in the order: zwitterion > anion > cation > enol, provided that bands

FIG. 1. *The ultraviolet absorption spectra of* . . . . . 3-*methoxypyridine at* pH 7, —·—·— *the cation* (pH 2), *and* — — — *the anion* (pH 13) *of* 3-*hydroxypyridine, and* ——— 3-*hydroxypyridine* 1-*methohydroxide* (i.e. V) *in water* (pH. 7), *and* —··—··— *in dioxan.*



of corresponding intensity are compared. In the 4-hydroxy-derivatives of pyridine and pyridazine low-intensity bands or shoulders appear in the spectra of the enol and the anion on the long-wave side of the main high-intensity bands (Table 1; Fig. 2). The main bands are comparable in intensity to the single measurable absorption bands of the cation and zwitterion forms, and their positions follow the general sequence given above (Fig. 2). The various charged species of the 4-hydroxy-derivatives of pyridine and pyridazine absorb at shorter wavelengths and with higher intensities than the corresponding species of the isomeric derivatives (Table 1; Figs. 1 and 2). A similar contrast between the spectra of 4-hydroxypyrimidine and those of its isomers is not observed, owing to structural and tautomeric complexities, which lead also, in the case of these and other hydroxydiazines, to some deviations from the generally observed order in the positions of the long-wave band of charged species.

The effect of changing from aqueous to non-polar solvents on the position of the long-wavelength band of the zwitterionic or amide form of the hydroxypyridines is profound (Table 2; Fig. 1). The absorption of 1-methyl-2- and -4-pyridone shifts 1000 cm.$^{-1}$ towards the red region on change from aqueous to *cyclo*hexane solution, whilst that of the 3-compound (V; R = Me) moves 3000 cm.$^{-1}$ towards the red region on changing from aqueous to dioxan solution, this zwitterion being insoluble in *cyclo*hexane. The absorption

TABLE 2. *The effect of solvents on the position of the first* $\pi \longrightarrow \pi$ *band in the spectra of the* N*-methyl derivatives of the hydroxypyridines (zwitterionic forms).*

Solvent		1-Methyl-2-pyridone	1-Methyl-3-pyridoxide ion	1-Methyl-4-pyridone
Dioxan–water	0%	297	320	260
	30%	298	323·5	261
	60%	300	328	262
	80%	302	332	263
	95%	304	340·5	264·5
	100%	307	356	265·5
Ethanol		300	328	262
*cyclo*Hexane		308·5	*a*	266·5

[a] Insoluble.

of the methoxy-derivatives of the azines, which have fixed enolic forms, undergoes only small blue or red shifts on changing from aqueous to *cyclo*hexane solution (Table 1; Fig. 3). The wavelength of the absorption maximum of the methoxy-azine can change considerably, owing to the appearance of vibrational fine structure in the spectrum measured in *cyclo*hexane, but the position of the band origin, in general, does not change greatly (Fig. 3).

The relative positions and intensities of the long wavelength bands in the spectra of 2- and 4-hydroxypyridine and their *N*-methyl derivatives have been interpreted by means of qualitative valence-bond theory.[2] If the amide structures (IVb) and (VIb) predominate in the ground states of 2- and 4-hydroxypyridine, respectively, and if the excited states are

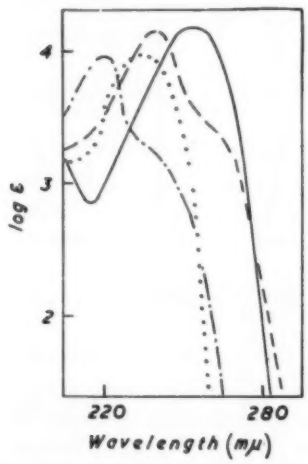


FIG. 2. *The ultraviolet absorption spectra of* — · — · — *4-methoxypyridine at* pH 9, ... *the cation* N*-hydrochloric acid,* — — — *the anion* (pH 13), *and* ——— *the zwitterion or amide form of 4-hydroxypyridine* (pH 7).

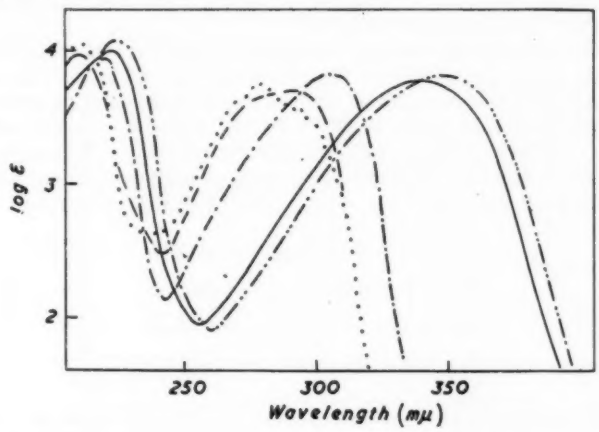
made up largely from the zwitterionic structures (IVa) and (VIa), respectively, the separation of charge during the electronic excitation is greater in 4- than in 2-hydroxypyridine. The greater the separation of charge, the larger is the energy difference between the ground and the excited state, so that 4-hydroxypyridine should absorb at shorter wavelengths than the 2-isomer, as observed.[2] The greater separation of charge should result also in a larger transition moment, and the ratio of the intensities of the long-wavelength band in the spectra of 4- and 2-hydroxypyridine should approximately equal the ratio of the squares of the distances between the charged centres in (VIa) and (IVa), respectively.[2] The ratio [2] of the squares of the distances between the charged centres is 2·86, whilst the ratio of the oscillator strengths of the long-wavelength transitions in the spectra of 4- and 2-hydroxypyridine is 2·53, and of the corresponding *N*-methyl derivatives is 2·98 (Table 1). For the analogous cases of 4- and 3-hydroxypyridazine, and 1- and 3-methyl-4-pyrimidone, the ratios of the oscillator strengths are 4·16 and 3·32, respectively (Table 1), in poorer

[2] Berson, *J. Amer. Chem. Soc.*, 1953, **75**, 3521.

agreement with the ratio of the squares of the distances between the charged centres.

The foregoing valence-bond interpretation of the relative intensities and positions of the first absorption band in the spectra of the zwitterionic or amide form of 2- and 4-hydroxypyridine requires that the excited state of the transitions should be more polar than the ground state. The red shift in the spectra of 1-methyl-2- and -4-pyridone observed on changing from aqueous to *cyclo*hexane solution suggests, on the contrary, that the ground state is more polar than the excited state. In aqueous solution the polar ground state is more stabilised by solvation than is the excited state, and the transition energy is increased relative to that measured in *cyclo*hexane where the solvation energy of a polar state is

FIG. 3. *The ultraviolet absorption spectra of — — — the neutral molecule of 2-methoxypyrazine in water* (pH 7), *and . . . . . in* cyclo*hexane, — · — · — the cation of 2-methoxypyrazine* (5N-*sulphuric acid*), ——— *the cation of 2-hydroxypyrazine* (10N-*sulphuric acid*), *and — · · — · · — the cation of 1-methyl-2-pyrazone* (10N-*sulphuric acid*).

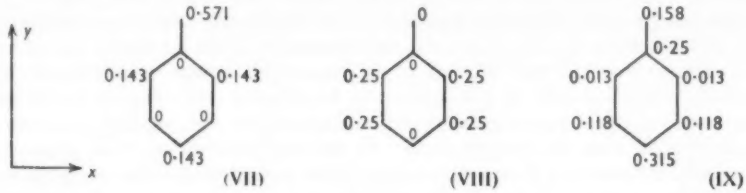


much smaller. Dipole-moment measurements also show that the ground state is highly polar, the moments [3] of 1-methyl-2- and -4-pyridone being 4·15 and 6·9 D, respectively. Moreover, the valence-bond treatment cannot be generalised to cover the 1 : 3-hydroxy-azines. The "*meta*-quinonoid" structure (Vb), analogous to (IVb) and (VIb), cannot predominate in the ground state of the 3-compound (V), which, in view of its salt-like character, is more adequately described by the zwitterion structure (Va).

Molecular-orbital theory offers a more general explanation of the relative positions and intensities of the absorption bands in the spectra of the 1 : 3- as well as of the 1 : 2- and 1 : 4-hydroxy-azines, and it accounts for the shifts of the bands observed on passing from one charged species to another. The hydroxy-group, and more particularly the negatively-charged oxy-group, conjugates with an azine nucleus, the lone-pair electrons of the oxygen atom being delocalised over the ring. The lone-pair electrons of oxygen enter a π-orbital which corresponds to the non-bonding molecular orbital in the analogous carbanion, the benzyl ion, and, being non-bonding electrons, they are loosely held and are readily promoted on absorption of light to an unoccupied π-orbital. The highest occupied and lowest unoccupied π-orbitals of a hydroxy-azine can be treated, respectively, as the non-bonding molecular orbital and the lowest unoccupied π-orbitals of the benzyl anion perturbed by the substitution of an oxygen atom at the exocyclic position and by aza-substitution in the ring. The charge distributions in the non-bonding molecular orbital (ψ_N) and the two lowest unoccupied π-orbitals (ψ_I and ψ_{II}) of the benzyl anion are given

[3] Albert and Phillips, *J.*, 1956, 1294.

in (VII), (VIII), and (IX), respectively. The energies of the orbitals ψ_N, ψ_I, and ψ_{II} are



(VII) (VIII) (IX)

0, β, and 1·26β respectively, where β is the carbon–carbon resonance integral. Electronic transitions from ψ_N (VII) to ψ_I (VIII) and to ψ_{II} (IX) are allowed with transition energies of β and 1·26β, respectively, and with transition moments along the x and y axes of (VII), respectively. For absorption in the 300-mμ region, the theoretical oscillator strength of the first transition, $\psi_N \longrightarrow \psi_I$, is 0·15, and of the second transition, $\psi_N \longrightarrow \psi_{II}$, is 0·84, the ratio of the two oscillator strengths being 5·5.

On substitution of an oxygen atom at the exocyclic position and aza-substitution in the ring of the benzyl anion, the energies of the orbitals ψ_N, ψ_I, and ψ_{II} are changed, according to first-order perturbation theory, by an amount proportional to the fractional charges at the positions of substitution, given in (VII), (VIII), and (IX), respectively, and to the increment in the Coulomb integral of the substituent relative to carbon ($\Delta\alpha$). Thus, the energies of the first electronic transition, $\psi_N \longrightarrow \psi_I$, in the enol, cation, anion, and zwitterion form of 3-hydroxypyridine, E_{IE}, E_{IC}, E_{IA}, and E_{IZ} respectively, are

$$E_{IE} = \beta + 0{\cdot}571\Delta\alpha_{OH} - 0{\cdot}25\Delta\alpha_N \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$E_{IC} = \beta + 0{\cdot}571\Delta\alpha_{OH} - 0{\cdot}25\Delta\alpha_{NH^+} \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

$$E_{IA} = \beta + 0{\cdot}571\Delta\alpha_{O^-} - 0{\cdot}25\Delta\alpha_N \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

$$E_{IZ} = \beta + 0{\cdot}571\Delta\alpha_{O^-} - 0{\cdot}25\Delta\alpha_{NH^+} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

where $\Delta\alpha_{OH}$ and $\Delta\alpha_{O^-}$ are the increments in the Coulomb integrals of a neutral and a negatively-charged oxygen atom, respectively, relative to carbon, and $\Delta\alpha_N$ and $\Delta\alpha_{NH^+}$ are the corresponding increments of a neutral and a positively charged nitrogen atom, respectively. From the free energies of ionisation of the hydroxy-azines it has been found [4] that $\Delta\alpha_N = 0{\cdot}6\beta$ and $\Delta\alpha_{NH^+} = 2{\cdot}5\beta$, whilst it is probable that $\Delta\alpha_{OH} \simeq \beta$, and $\Delta\alpha_{O^-} \simeq 0$. The precise values are not very significant, but it is important that $\Delta\alpha_{NH^+} > \Delta\alpha_N$ and that $\Delta\alpha_{OH} > \Delta\alpha_{O^-}$. These inequalities show (equations 1—4) that the energies of the first electronic transition, $\psi_N \longrightarrow \psi_I$, in the charged species of 3-hydroxypyridine follow the order $E_{IE} > E_{IC} > E_{IA} > E_{IZ}$ (Fig. 4), as is found experimentally (Fig. 1; Table 1). The observed transition energies are not obtained quantitatively from eqns. (1)—(4) and the given Coulomb parameters, and, conversely, consistent values for the differences ($\Delta\alpha_{NH^+} - \Delta\alpha_N$) and $\Delta\alpha_{OH} - \Delta\alpha_{O^-}$) cannot be derived from the observed energies and eqns. (1)—(4), or the analogous equations for the other hydroxy-azines. Eqns. (1)—(4) and their analogues are ill-conditioned, owing to the very approximate nature of the theory employed, but they indicate correctly the qualitative order of the transition energies in the charged species of the various hydroxy-azines.

The energy of the second electronic transition, $\psi_N \longrightarrow \psi_{II}$, in a given charged form of 3-hydroxypyridine, E_{II}, is given by

$$E_{II} = 1{\cdot}26\beta + 0{\cdot}413\Delta\alpha_o - 0{\cdot}118\Delta\alpha_n \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

where $\Delta\alpha_o$ is either $\Delta\alpha_{OH}$ or $\Delta\alpha_{O^-}$, and $\Delta\alpha_n$ is either $\Delta\alpha_N$ or $\Delta\alpha_{NH^+}$, depending upon the charged species considered. Eqn. (5) indicates that the energies of the second transition

[4] Mason, *J.*, 1958, 674.

in the charged forms of 3-hydroxypyridine should follow the same order as those of the first transition, though the differences in transition energy between one charged species and another should be smaller (Fig. 4), as is found (Fig. 1; Table 1).

In 2-hydroxypyridine the energies of the first, $\psi_N \longrightarrow \psi_I$, and the second, $\psi_N \longrightarrow \psi_{II}$, electronic transitions, E_I and E_{II}, respectively, are given by

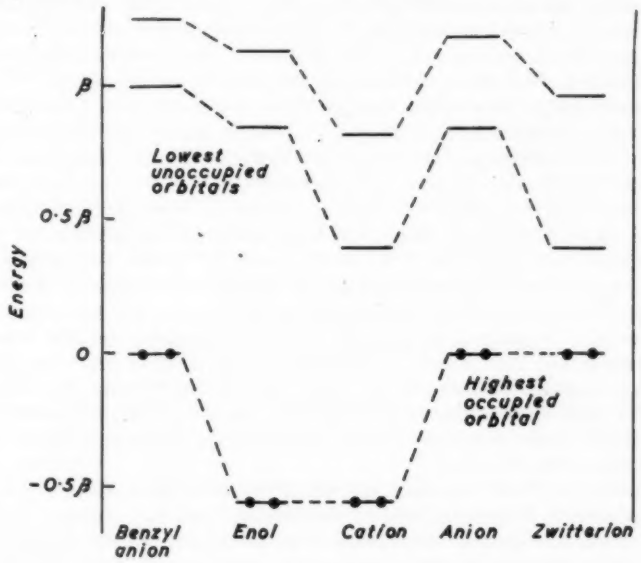
$$E_I = \beta + 0{\cdot}571\Delta\alpha_o - 0{\cdot}107\Delta\alpha_n \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

and

$$E_{II} = 1{\cdot}26\beta + 0{\cdot}413\Delta\alpha_o + 0{\cdot}130\Delta\alpha_n \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

The charged species of 2-hydroxypyridine should have energies for the first transition, from eqn. (6), lying in the sequence $E_{IB} > E_{IC} > E_{IA} > E_{IZ}$, and for the second transition, from eqn. (7), in the order $E_{IIC} > E_{IIB} > E_{IIZ} > E_{IIA}$, whilst the spectrum of a given

FIG. 4. *The energies of the highest occupied and the lowest unoccupied orbitals of the enol, cation, anion, and zwitterion of 3-hydroxypyridine derived by the first-order perturbation of the corresponding orbitals of the benzyl anion.*



charged form should be displaced as a whole to shorter wavelengths relative to that of the corresponding charged species of 3-hydroxypyridine. The observed absorption bands follow these orders, though the enolic form, as represented by 2-methoxypyridine in neutral solution, may be anomalous since a second absorption maximum at short wavelengths could not be measured (Table 1).

In 4-hydroxypyridine the energies E_I and E_{II} of the electronic transitions, $\psi_N \longrightarrow \psi_I$ and $\psi_N \longrightarrow \psi_{II}$ respectively, are given by

$$E_I = \beta + 0{\cdot}571\Delta\alpha_o + 0{\cdot}143\Delta\alpha_n \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

and

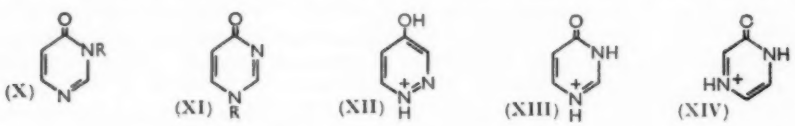
$$E_{II} = 1{\cdot}26\beta + 0{\cdot}413\Delta\alpha_o - 0{\cdot}172\Delta\alpha_n \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (9)$$

The energy of the second transition becomes less than that of the first if $\Delta\alpha_n > 0{\cdot}7\beta$ when the oxygen atom is negatively charged, since $\Delta\alpha_{O^-} \simeq 0$, and at a still smaller value of $\Delta\alpha_n$ when the oxygen atom is neutral. In the cationic and the zwitterionic form of 4-hydroxypyridine the nitrogen atom is positively charged, and as $\Delta\alpha_{NH^+} = 2{\cdot}5\beta$, the single

high-intensity absorption band of these species is due to the second transition, $\psi_N \longrightarrow \psi_{II}$. The nitrogen atom is formally neutral in the enolic and anionic form, and since $\Delta\alpha_N = 0{\cdot}6\beta$, the energy of the first transition should be slightly less than that of the second, thus accounting for the low-intensity shoulders on the long-wavelength side of the main high-intensity band in the spectra of these species (Fig. 2; Table 1). The orders of the energies of these transitions, $E_{IE} > E_{IA}$ and $E_{IIE} > E_{IIC} > E_{IIA} > E_{IIZ}$, agree with the positions of the shoulders and of the main bands, respectively (Table 1). For a given charged form the shoulder should lie (eqns. 1—9) at a shorter wavelength and the main absorption band at a longer wavelength than the bands due to the first and the second transition respectively in the spectra of the corresponding charged species of either 2- or 3-hydroxypyridine, as is observed (Table 1).

In the electronic spectrum of the benzyl anion the intensity of the second transition, $\psi_N \longrightarrow \psi_{II}$, should be some 5·5 times greater than that of the first transition, $\psi_N \longrightarrow \psi_I$, and to a first approximation the intensity ratio should be the same in the spectra of the hydroxy-derivatives of the monocyclic azines. Apart from the cationic forms of 2- and 3-hydroxypyridine, the short wavelength absorption bands of the hydroxy-azines studied are more intense than the long wavelength bands, though the ratio of the intensities is generally less than the theoretical value of 5·5 (Table 1). Aza-substitution of a ring position in the benzyl anion has the effect of distorting the orbitals, ψ_N, ψ_I, and ψ_{II}. In particular charge is drawn to the position of the nitrogen atom in the orbital ψ_N from other positions. Thus, in 3-hydroxypyridine charge is drawn from the 2-, 4-, 6-, and exocyclic positions to, the nitrogen atom in orbital ψ_N, with the result that an electronic transition to orbital ψ_I is increased and to orbital ψ_{II} is decreased in intensity. A similar intensity change should occur in 2-hydroxypyridine, and the changes should be even more pronounced in the zwitterion and, more particularly, the cation form of these compounds where the nitrogen atoms are positively charged, as is observed (Table 1) With 4-hydroxypyridine the attraction of charge to the nitrogen atom in the ground state should have the contrary effect of diminishing the intensity of the first transition, $\psi_N \longrightarrow \psi_I$, and enhancing that of the second, $\psi_N \longrightarrow \psi_{II}$. Appearing as a shoulder in the spectrum, the first transition is of uncertain intensity, but the extinction coefficient at the point of inflection (Fig. 2) being taken as an approximate measure, which represents an upper value, it is found that the ratio of the intensities of the second to the first transition in 4-hydroxypyridine is the highest of those for all the hydroxy-azines studied, exceeding the theoretical value of 5·5 in the case of the anionic form (Table).

The interpretation of the electronic spectra of the hydroxy-diazines is complicated by the possible existence, in general, of two zwitterionic and two cationic forms of these compounds. There is a unique zwitterionic form of 2- and of 5-hydroxypyrimidine by symmetry, but the 4-isomer has the two zwitterionic or amide forms (X; R = H) and (XI; R = H) which co-exit in the ratio of about 2 : 1 in neutral aqueous solution.[4,5] In



3- and 4-hydroxypyridazine and 2-hydroxypyrazine the predominant zwitterion or amide species is formed by the bonding of the tautomeric hydrogen atom to the ring nitrogen atom α or γ to it.[1] The cations of the hydroxypyridazines are formed by the protonation of the oxygen atom of the zwitterion [4] (*e.g.* XII), but in those of 2- and 4-hydroxypyrimidine a nitrogen and not the oxygen atom is protonated [5] (*e.g.* XIII). The cation of 2-hydroxypyrazine (XIV) resembles the latter type, since its spectrum resembles that of the *N*-methyl but not that of the *O*-methyl derivatives (Fig. 3).

[5] Brown, Hoerger, and Mason, *J.*, 1955, 211.

The energies E_I and E_{II}, of the first two transitions in the spectra of the anionic and enolic form of 2-hydroxypyrazine are given by

$$E_I = \beta + 0{\cdot}571\Delta\alpha_O - 0{\cdot}357\Delta\alpha_N \quad . \quad . \quad . \quad . \quad . \quad . \quad (10)$$

and

$$E_{II} = 1{\cdot}26\beta + 0{\cdot}413\Delta\alpha_O + 0{\cdot}012\Delta\alpha_N \quad . \quad . \quad . \quad . \quad . \quad . \quad (11)$$

whilst for the zwitterion the corresponding expressions are

$$E_I = \beta + 0{\cdot}571\Delta\alpha_{O^-} - 0{\cdot}107\Delta\alpha_{NH^+} - 0{\cdot}25\Delta\alpha_N \quad . \quad . \quad . \quad . \quad (12)$$

and

$$E_{II} = 1{\cdot}26\beta + 0{\cdot}413\Delta\alpha_{O^-} + 0{\cdot}130\Delta\alpha_{NH^+} - 0{\cdot}118\Delta\alpha_N \quad . \quad . \quad . \quad (13)$$

and for the cation (XIV)

$$E_I = \beta + 0{\cdot}571\Delta\alpha_{O^-} - 0{\cdot}357\Delta\alpha_{NH^+} \quad . \quad . \quad . \quad . \quad . \quad . \quad (14)$$

and

$$E_{II} = 1{\cdot}26\beta + 0{\cdot}413\Delta\alpha_{O^-} + 0{\cdot}012\Delta\alpha_{NH^+} \quad . \quad . \quad . \quad . \quad . \quad (15)$$

Eqns. (10)—(15) indicate that the energies of the first transition in the spectra of the charged species of 2-hydroxypyrazine should follow the sequence, $E_{IE} > E_{IA} > E_{IZ} > E_{IC}$, whilst the energies of the second transition should lie in the order $E_{IIE} > E_{IIZ} > E_{IIC} > E_{IIA}$, as is found experimentally (Table 1).

Similar expressions can be derived for the energies of the first two transitions in the spectra of the other hydroxy-diazines. For the case of 3-hydroxypyridazine the predicted sequences of transition energies are $E_{IE} > E_{IC} > E_{IA} > E_{IZ}$ and $E_{IIC} > E_{IIE} > E_{IIZ} > E_{IIA}$. These orders are observed, apart from the first absorption band of the zwitterion which lies at a shorter wavelength than that of the anion, and the second band of the enol, as represented by 3-methoxypyridazine in neutral solution, which was not measurable (Table 1). The patterns of the absorption bands in the spectra of the charged species of 4-hydroxypyridazine and 4-hydroxypyridine are very similar (Table 1). The equations for the transition energies in the case of the former compound are

$$E_I = \beta + 0{\cdot}571\Delta\alpha_O + 0{\cdot}143\Delta\alpha_n - 0{\cdot}25\Delta\alpha_N \quad . \quad . \quad . \quad . \quad . \quad (16)$$

and

$$E_{II} = 1{\cdot}26\beta + 0{\cdot}413\Delta\alpha_O - 0{\cdot}172\Delta\alpha_n - 0{\cdot}118\Delta\alpha_N \quad . \quad . \quad . \quad . \quad (17)$$

As in the case of 4-hydroxypyridine the first transition is perceptible only in the spectra of the enolic and anionic species of 4-hydroxypyridazine, but the additional nitrogen atom in the latter lowers the energy of the first transition more than that of the second (eqns. 8, 9, 16, 17), so that the absorption due to the first transition appears as a discrete band (Table 1), and not just as a shoulder on the side of the main absorption band (Fig. 2). The spectrum of a given charged form of 4-hydroxypyridazine should be displaced to longer wavelengths relative to that of the corresponding species of 4-hydroxypyridine (eqns. 8, 9, 16, 17), and the sequences of transition energies should be the same in both compounds, as is observed (Table 1).

The predicted orders of the transition energies in the case of 2-hydroxypyrimidine are $E_{IE} > E_{IA} > E_{IZ} > E_{IC}$ and $E_{IIC} > E_{IIE} > E_{IIZ} > E_{IIA}$. The absorption maxima due to the second transition in the enol and the cation could not be measured, but otherwise these orders are supported by the experimental data (Table 1). In neutral aqueous solution 4-hydroxypyrimidine exists in two zwitterionic or amide forms [4,5] which can be studied separately as the respective derivatives, 1- and 3-methyl-4-pyrimidone, (XI; R = Me) and (X; R = Me). The expected sequences of transition energies are $E_{IE} > E_{I(XI)} > E_{IC} > E_{IA} > E_{I(X)}$ and $E_{IIE} > E_{II(X)} > E_{IIA} > E_{IIC} > E_{II(XI)}$. The band due to the first transition in 1-methyl-4-pyrimidone (XI; R = Me) is overlaid by the high-intensity absorption due to the second transition,[5] but apart from this the first sequence is found experimentally (Table 1). However, the data show that the transition energies of the anion and the cation form lie in the order contrary to that expected from the second sequence, which is otherwise followed (Table 1). The spectrum of a given charged form of 5-hydroxypyrimidine should be displaced to longer wavelengths relative to that of the corresponding

species of 3-hydroxypyridine, and the sequences of the transition energies should be the same in both compounds, as is found experimentally (Table 1).

The molecular-orbital theory of the light absorption of the hydroxy-azines is consistent with the wavelength shifts observed in the spectra of the zwitterionic and enolic forms of the compounds on changing from an aqueous to a non-polar solvent. In the ground state, according to the present approximation, the nitrogen atom of the zwitterion (V; R = Me) carries a unit positive charge, and the oxygen atom 0·571 of a negative charge, the remaining negative charge being distributed over the carbon atoms α and γ to the carbon carrying the oxygen atom (VII). In the first excited state the positive charge on the nitrogen atom is reduced to 0·75, and the oxygen atom is neutral, the 0·75 of a negative charge being shared between the carbon atoms α and β to that carrying the oxygen (VIII). The first excited state should be less polar than the ground state, therefore, in conformity with the large red shift (3000 cm.$^{-1}$) in the first absorption band of the species (V; R = Me) observed on passing from aqueous to dioxan solution (Table 2).

The ground state of 1-methyl-2-pyridone is less polar than that of the 3-isomer, the nitrogen atom carrying 0·857 of a positive charge, and the corresponding negative charge being distributed over the oxygen atom and the carbon atoms α and γ to the carbon atom carrying it (VII). However, the charge distributions in the first excited state of 1-methyl-2-pyridone and the 3-isomer are the same, namely, 0·75 of a positive charge on the nitrogen atom with the corresponding negative charge shared between the carbon atoms α and β to the carbon atoms carrying the oxygen atom (VIII). The decrease in polarity during the transition, $\psi_N \longrightarrow \psi_I$, should be smaller in 1-methyl-2-pyridone than in the 3-isomer, which is consistent with the smaller red shift (1000 cm.$^{-1}$) in the first absorption band of 1-methyl-2-pyridone found on changing from aqueous to *cyclo*hexane solution (Table 2). The decrease in the polarity of 1-methyl-4-pyridone during the transition $\psi_N \longrightarrow \psi_{II}$ involving a change in charge distribution from (VII) to (IX), should also be smaller than that of the 3-isomer during the transition $\psi_N \longrightarrow \psi_I$ in conformity with the smaller red shift of 1000 cm.$^{-1}$ (Table 2).

The enolic forms of the hydroxy-azines should be more polar in the excited state than in the ground state, and the absorption bands of this species might be expected to show blue shifts on changing from aqueous to non-polar solvents. The methoxy-azines, with fixed enolic forms, give only small shifts, which are both towards the red and the blue region, on passing from aqueous to *cyclo*hexane solution (Table 1; Fig. 3). In the methoxy-azines it is probable that the stabilisation of the polar excited state by solvation in aqueous solution is offset by the stabilisation of the ground state, owing to hydrogen-bonding with the water molecules. In the present view it is the lone-pair electrons of the oxygen atom which are active in the first two electronic transitions of the hydroxyazines, and the energy of these electrons, which readily engage in hydrogen-bonding, should be particularly sensitive to the nature of the solvent employed.

Experimental

Materials.—The pyridazine derivatives were kindly supplied by Drs. K. Eichenberger, R. Rometsch, and J. Druey,[6] and 5-hydroxypyrimidine by Dr. J. F. W. McOmie. 2- and 4-Hydroxypyrimidine and their *N*- and *O*-methyl derivatives were prepared as in Brown, Hoerger, and Mason,[5] and the remaining compounds as in Albert and Phillips.[3]

Spectra.—These were measured with Hilger Uvispek Quartz Spectrophotometers, the solvents listed in Tables 1 and 2 being used.

The author is indebted to the Australian National University for a Research Fellowship and to the Royal Society for the provision of a spectrophotometer.

Chemistry Department, The University, Exeter. [*Received, August* 21*st*, 1958.]

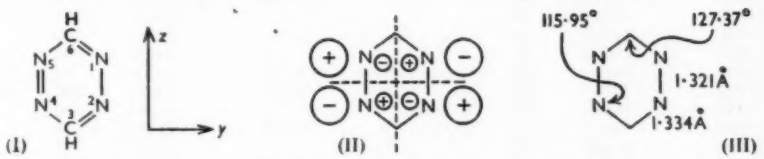
[6] Eichenberger, Rometsch, and Druey, *Helv. Chim. Acta*, 1954, **37**, 1298; 1956, **39**, 1755.

248. *The Electronic Spectra of N-Heteroaromatic Systems. Part IV.* The Vibrational Structure of the $n \longrightarrow \pi$ Band of* sym*-Tetrazine.*

By S. F. Mason.

The vibrational structure of the visible absorption spectrum of *sym*-tetrazine has been measured in the vapour, together with that of the 3 : 6-dideutero-derivative; in *cyclo*hexane at room temperature, together with that of the 3 : 6-dimethyl derivative; and in a 5 : 1-*iso*pentane–methyl-*cyclo*hexane glass at 77° K. For the vapour of *sym*-tetrazine the strongest band is the 0–0, which shifts towards the red end of the spectrum in the dideutero-derivative; the observed upper-state progessions are short, indicating the electronic transition, whilst of low oscillator strength, is allowed that by symmetry, and that there is little change in the size of the molecule on excitation, although the molecular zero-point energy increases. The particular vibrations active in the electronic transition suggest that *sym*-tetrazine assumes a more regular hexagonal shape on excitation.

THE monocyclic *N*-heteroaromatic compound *sym*-tetrazine (I) has an unusual absorption spectrum in the visible region. Curtius, Darapsky, and Muller remarked upon the sharpness of the absorption and listed qualitatively five main bands.[1] Koenigsberger and and Vogt described [2] the visible absorption of *sym*-tetrazine as " a new kind of molecular spectrum," since, for the first time, bands of molecular origin were observed which appeared to be as sharp as the lines of atomic spectra. These workers measured [2] the positions of



(I) (II) (III)

some thirty-five absorption bands of *sym*-tetrazine vapour in the visible region, which is about half the number that have been now recorded by use of the relatively low resolution of the Cary spectrophotometer. The vibrational band structure of the visible absorption spectrum of *sym*-tetrazine in *cyclo*hexane at room temperature and in a 5 : 1 *iso*pentane–methyl*cyclo*hexane glass at 77° K has been measured also, and for the purposes of comparison the spectra of 3 : 6-dideuterotetrazine in the vapour and of 3 : 6-dimethyltetrazine in *cyclo*hexane have been recorded. The results obtained are listed in Tables 1—3, and the spectra of *sym*-tetrazine are given in the Figure.

The general features of the visible absorption of *sym*-tetrazine, and of the band of longest wavelength in the spectra of the monocyclic azines generally, suggest [3] that the absorption is due to the transition of a non-bonding electron from a lone-pair orbital of the nitrogen atoms to a π-orbital of the ring. As with most non-polar chromophores, the absorption of *sym*-tetrazine shows a small red shift on change from the vapour to *cyclo*hexane solution (Tables 1 and 2), which is due to the momentary polarisation of the solvent by the transition dipole of the solute,[4] but on change from *cyclo*hexane to aqueous solution the absorption undergoes a considerable blue shift of some 1000 cm.$^{-1}$ (Table 2), a feature which is characteristic of $n \longrightarrow \pi$ transitions.[5,6] In aqueous solution the lone-pair

* Part III, preceding paper.

[1] Curtius, Darapsky, and Muller, *Ber.*, 1907, **40**, 84.
[2] Koenigsberger and Vogt, *Physikal. Z.*, 1913, **14**, 1269.
[3] Part I, *J.*, 1959, 1240.
[4] Bayliss and McRae, *J. Phys. Chem.*, 1954, **58**, 1002.
[5] Kasha, *Discuss. Faraday Soc.*, 1950, **9**, 14.
[6] McConnell, *J. Chem. Phys.*, 1952, **20**, 700.

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electrons of *sym*-tetrazine are engaged in hydrogen bonding, and the promotion of such an electron to a π-orbital requires the provision of additional energy to break the hydrogen bonds.

Further, the vibrational fine structure of the visible spectrum of *sym*-tetrazine is entirely lost in aqueous solution, though the main features of the dominant progression observed in the vapour are retained in *cyclo*hexane solution (Fig.). The solvation cage of a solute in the ground state becomes strained when the solute absorbs radiation and

TABLE 1. *The frequencies (ν) and the optical densities (d) of the bands in the visible absorption spectra of* sym*-tetrazine and deuterated* sym*-tetrazine in the vapour at room temperature.*

Dideuterotetrazine	Tetrazine			Dideuterotetrazine	Tetrazine		
ν (cm.$^{-1}$)	ν (cm.$^{-1}$)	10^3d	Assign.	ν (cm.$^{-1}$)	ν (cm.$^{-1}$)	10^3d	Assign.
17320	17320	34		19800	19910	103	
17390	17410	66	A 1—0	19920	19940	168	
17520	17540	40		19950	20010	120	
17640	17690	36		—	20070	128	
17850	17810	40		20050	20110	120	
17870	17860	60		20130	20190	114	
17950	17910	66		20190	20250	181	0—3 A
17980	17970	76		20280	20340	409	D_4
18040	18050	164		20420	20410	114	
18120	18135	658	0—0	—	20460	119	
18240	18195	114	D_1	20480	20490	194	
18280	18280	284		—	20530	155	
18370	18340	86		20610	20620	108	
18350	18430	120		20650	20650	137	
18480	18480	60		20730	20720	103	
18530	18550	86		—	20760	111	
18550	18615	86		20810	20810	100	
18630	18650	86		—	20900	96	
18650	18680	111		20880	20950	92	0—4 A
18730	18760	256		20970	20980	205	D_5
18810	18830	629	0—1 A	—	21040	100	
18900	18910	447	D_2	21130	21160	114	
18990	18990	276		—	21200	87	
19040	19070	194		21170	21230	92	
19160	19140	177		—	21320	78	
19230	19230	137		21290	21340	81	
19250	19250	149		—	21420	76	
19330	19290	131		21420	21470	66	
19350	19360	111		—	21510	66	
19390	19400	131		—	21610	92	
19430	19470	208		21560	21650	71	0—5 A
19500	19540	377	0—2 A	21680	21760	76	
19590	19620	594	D_3	—	21880	66	
19640	19690	208		—	21910	66	
19690	19780	255					
19730	19850	190					

TABLE 2. *The visible absorption spectra of* sym*-tetrazine and* 3 : 6*-dimethyltetrazine in water and in* cyclo*hexane at room temperature. Values in italics refer to shoulders or inflexions.*

sym-Tetrazine						3 : 6-Dimethyltetrazine			
$\nu_{max.}$ (cm.$^{-1}$)	$\varepsilon_{max.}$	$\nu_{max.}$ (cm.$^{-1}$)	$\varepsilon_{max.}$	$\nu_{max.}$ (cm.$^{-1}$)	$\varepsilon_{max.}$	$\nu_{max.}$ (cm.$^{-1}$)	$\varepsilon_{max.}$	$\nu_{max.}$ (cm.$^{-1}$)	$\varepsilon_{max.}$
In *cyclo*hexane									
17160	21·5	*18870*	*262*	*20200*	*250*	16780	69	18660	662
17880	611	19350	625	20810	139	17300	644	19120	524
18020	*112*	*19530*	*300*	*20920*	*109*	17810	832	*19530*	*391*
18560	829	20110	543	21490	55	18300	750	*20040*	*271*
				21620	12				
In water									
		19600	362			19340	365		

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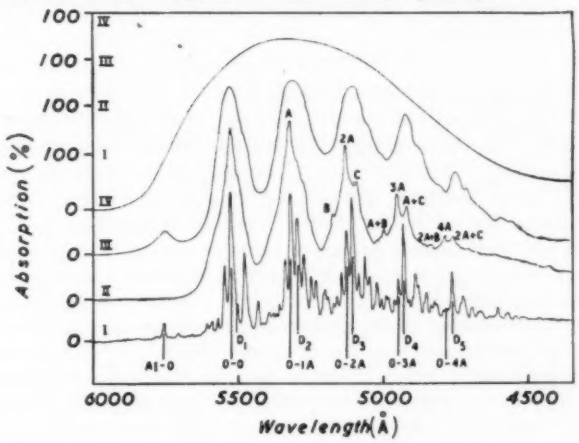
changes in shape and in electron distribution. If the solvation forces are weak dispersion interactions, as in *cyclo*hexane solution, the strain is not large unless the solute undergoes a considerable change in size on excitation, and much of the vibrational structure observed

TABLE 3. *The visible absorption spectrum of* sym-*tetrazine in* 5 : 1-iso*pentane–methylhexane at* 77° K. *Values in italics refer to shoulders of inflexions.*

$\nu_{max.}$ (cm.$^{-1}$)	$\varepsilon_{max.}$	Assignment	$\nu_{max.}$ (cm.$^{-1}$)	$\varepsilon_{max.}$	Assignment
17970	1090	0—0	19760	183	—
18060	*640*	—	19850	230	A + B
18665	1210	A (695 cm.$^{-1}$)	20045	404	3A
18730	*695*	—	20180	337	A + C
18820	*490*	—	20310	171	2B
19175	275	B (1205 cm.$^{-1}$)	20425	167	—
19355	1110	2A	20525	167	2A + B
19430	*503*	—	20730	200	4A
19500	496	C (1530 cm.$^{-1}$)	20860	200	2A + C

in the spectrum of the vapour should be retained. *sym*-Tetrazine does not undergo any major change in size on excitation in the visible region, since in the vapour the 0–0 vibrational transition gives rise to the most intense absorption band of the whole progression, and the progression itself is short (Table 1; Fig.).

The visible absorption spectrum of sym-*tetrazine*: I, *at room temperature in the vapour*; II, *at* 77° K *in a* 5 : 1 iso*pentane–methyl*cyclo*hexane glass*; III, *in* cyclo*hexane*; *and* IV, *in aqueous solution at room temperature. The wavelength scale refers to the spectrum of the vapour,* II *and* III *being shifted* 150 *and* 250 *cm.*$^{-1}$ *to higher frequencies, respectively, and* IV 750 *cm.*$^{-1}$ *to lower frequencies. The frequencies of the bands assigned in* I *and* II *are given in Tables* 1 *and* 3, *respectively.*



On the other hand, if the solvation forces are the stronger hydrogen-bonding and dipole–dipole interactions the solvation cage is subject [4] on the excitation of the solute, not only to packing strain, due to the change in the size of the excited molecule, but also to orientation strain, due to the redistribution of electrons, which changes the dipole moment of the solute, and, in the case of $n \longrightarrow \pi$ transitions, the capacity of the solute to form hydrogen bonds with the solvent. The time required for the electronic excitation of a molecule is very short compared with the relaxation time of the solvent, and the strain of the solvation cage following the excitation of the solute leads to a weakening of vibrational quantisation in the excited state, resulting in a broad absorption band without vibrational fine structure. The $n \longrightarrow \pi$ bands of solutes in aqueous solution are free from vibrational structure also because of hydrogen-bonding in the ground state. The infrared absorption band due to the O–H stretching vibration is greatly broadened on hydrogen-bonding, and the energy

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of the lone-pair electrons responsible for the bonding must cover a range of values, so that the electronic excitation of such a lone-pair electron to a π-orbital results in a broad and structureless absorption band.

The integrated intensity of the visible absorption of *sym*-tetrazine is small, the oscillator strength of the excitation being [3] 0·0042. The transition is allowed on symmetry grounds, however, as the spectra of *sym*-tetrazine at liquid-nitrogen and room temperatures show (Fig.) the presence of a strong 0–0 vibrational band between the 1–0 and the 0–1 bands. The weakened intensity may be accounted for on other grounds if the absorption is due to a $n \longrightarrow \pi$ transition. The lone-pair and the π-orbitals of *sym*-tetrazine are concentrated in different regions of space, so that transitions between them are improbable,[7] and only the " *s* " component of the *s*–*p* hybrid lone-pair orbital can contribute to the transition moment of a $n \longrightarrow \pi$ excitation.[8]

The $n \longrightarrow \pi$ band of *sym*-tetrazine lies at a longer wavelength than that of any other monocyclic azine, since on aza-substitution the highest occupied level of pyridine is raised in energy whilst the lowest unoccupied level is stabilised, these effects being most marked in the case of *sym*-tetrazine.[3] The lone-pair atomic orbitals of the nitrogen atoms in *sym*-tetrazine, particularly those of adjacent atoms, overlap one another and interact, giving rise to four lone-pair molecular orbitals, all of which are filled with electrons. The highest occupied lone-pair molecular orbital, ψ_g, is of the form (II), and it is given explicitly by

$$\psi_g = (\phi_2 - \phi_3 + \phi_5 - \phi_6)/2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where the ϕ's are lone-pair atomic orbitals of nitrogen. The lowest unoccupied π-orbital of tetrazine, ψ_e, is confined to the nitrogen atoms, having a node through the carbon positions, and it is given by

$$\psi_e = (\theta_2 - \theta_3 + \theta_5 - \theta_6)/2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where the θ's are $2p_x$ atomic orbitals of nitrogen.

The highest occupied and the lowest unoccupied molecular orbitals of *sym*-tetrazine, ψ_g and ψ_e, are similar in form, having the symmetries B_{3g} and A_u respectively in $\boldsymbol{D}_{2h}$, axes being taken as in (I). The orbitals differ, notably, in that ψ_g has no node in the plane of the molecule, so that an electronic transition from ψ_g to ψ_e is allowed ($A_g \longrightarrow B_{3u}$), with a transition moment perpendicular to the plane of the molecule. ψ_g is antibonding relative to a sp^2 lone pair atomic orbital of nitrogen and ψ_e is antibonding relative to a $2p$ atomic orbital, so that in the $n \longrightarrow \pi$ transition of *sym*-tetrazine there should be little change in the binding and the size of the molecule. There is no great change in the size of *sym*-tetrazine on excitation as the progression of vibrational bands in the spectrum is short and the vibrationless band is the most intense (Fig.). On passing from *sym*-tetrazine to 3 : 6-dideuterotetrazine the 0–0 vibration band in the visible spectrum of the vapour shifts some 15 cm.$^{-1}$ to lower frequencies (Table 1), suggesting that the zero-point energy and the binding of the molecule actually increase slightly on excitation. What appear to be sequences are observed on both the low- and the high-frequency side of the 0–0 band of the spectrum of the vapour (Fig.), indicating that some vibrational modes are increased in frequency and others decreased in the $n \longrightarrow \pi$ excitation of the tetrazine. The vibration responsible for the main progression in the visible spectrum of *sym*-tetrazine falls only from 725 cm.$^{-1}$ in the ground state to 695 cm.$^{-1}$ in the excited state (Tables 1 and 2).

Whilst there is little change in the overall size of the molecule, there should be minor changes in the shape of *sym*-tetrazine on excitation. In the ground state the molecule is not a regular hexagon, the bond lengths and angles determined by *X*-ray diffraction [9] being those of (III). In the excited state of the $n \longrightarrow \pi$ transition the 2—3 and 5—6 bonds of the tetrazine (I) should be weakened and lengthened, as ψ_e is more antibonding

[7] Platt, *J. Chem. Phys.*, 1951, **19**, 101.
[8] Orgel, *J.*, 1955, 121.
[9] Bertinotti, Giacomello, and Liquori, *Acta Cryst.*, 1956, **9**, 510.

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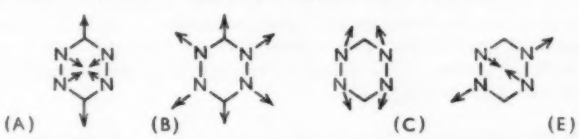
than ψ_g. The other bonds of the molecule should remain unaltered in the excited state, since a nodal plane, perpendicular to the molecular plane, passes through the positions 3 and 6 in ψ_e as in ψ_g (II). The CNN bond angle in the ground state [9] is 115·95°, indicating that the lone-pair electrons have some 40% of " *s* " character. In a $n \longrightarrow \pi$ transition the " *s* " character of the " hole " left by the promoted electron is shared by the remaining σ bond electrons of the nitrogen atoms, so that the CNN bond angles of *sym*-tetrazine increase towards 120° in the excited state. Thus the tetrazine should assume a shape near to that of a regular hexagon in the excited state of the $n \longrightarrow \pi$ transition.

In an electronic transition only the totally symmetric vibrations of a molecule give rise to progressions of bands in the spectrum.[10] The totally symmetric vibrations do not all appear in the spectrum with equal probability, for the nuclear positions and velocities do not change during the electronic jump, and so the equilibrium positions of the nuclei in the ground state are the turning points of the vibrations active in the excited state. Thus the totally symmetric vibrations which transform the ground-state shape (III) into a regular hexagon should appear the most prominently in the band structure of the $n \longrightarrow \pi$ transition.

sym-Tetrazine has four totally symmetric vibrations (symmetry A_g in D_{2h}), the forms of the three ring vibrations being given in (A), (B), and (C). The fourth A_g vibration is the C–H stretching mode, which is not active in the $n \longrightarrow \pi$ transition, for the band structure of the spectrum covers a range of little more than 3000 cm.$^{-1}$, the expected frequency of the mode. Of the A_g ring vibrations, mode (C), and more particularly mode (A), should be strongly active in the excited state of the $n \longrightarrow \pi$ transition, since they are modes appropriate for the transformation of the shape (III) of the ground state into a regular hexagon. At liquid-nitrogen temperatures, where the $n \longrightarrow \pi$ transition takes place from a vibrationless ground state, three main excited-state frequencies appear in the band structure of the spectrum, namely, 695, 1205, and 1520 cm.$^{-1}$ (Fig.; Table 3). These frequencies correspond to the modes (A), (B), and (C), respectively. The main progression in the spectrum is due to the ring angle bending mode (A), and the bands arising from the ring stretching mode (C) are more intense than those produced by the ring breathing mode (B) (Fig.; Table 3). In 1 : 4-dideutero- and 1 : 4-dimethyl-tetrazine the frequency of the vibration mode (A) falls to 690 and 510 cm.$^{-1}$ respectively, indicating that the carbon atom substituents move during this vibration.



In the ground state the ring angle bending mode (A) has a frequency of 725 cm.$^{-1}$, as is shown by the position of the 1–0 vibration band in spectra of the vapour and *cyclo*hexane solution at room temperature (Tables 1 and 2). The frequency is consistent with the assignment to the mode (A), as the corresponding vibration has a frequency of 675 cm.$^{-1}$ in *sym*-triazine [11] and of 606 cm.$^{-1}$ in benzene.[12] The ground-state frequencies of the ring breathing and stretching modes, (B) and (C), respectively, are not known, as the Raman spectrum of *sym*-tetrazine, in which the A_g vibrations would be active, could not be determined by the methods available, owing to the absorption of the molecule in the visible region. The ring stretching vibration (C) has frequencies of 1556 and 1596 cm.$^{-1}$ in *sym*-triazine [11] and benzene,[12] respectively, and in both of these molecules the ring breathing mode (B) has the frequency [11,12] of 992 cm.$^{-1}$. The frequency of 1530 cm.$^{-1}$ for the mode (C) in the excited state of the $n \longrightarrow \pi$ transition of *sym*-tetrazine is acceptable, therefore,

[10] Sponer and Teller, *Rev. Mod. Phys.*, 1941, **13**, 75.
[11] Lancaster and Colthup, *J. Chem. Phys.*, 1954, **22**, 1149; and private communication.
[12] Herzfeld, Ingold, and Poole, *J.*, 1946, 316.

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though the value of 1205 cm.$^{-1}$ for the mode (B) is rather large. Some of the vibrations of *sym*-tetrazine have increased frequencies in the excited state of the $n \longrightarrow \pi$ transition, as is shown by the appearance of sequences on the high-frequency side of the 0–0 band in the spectrum of the vapour (Fig.), and mode (B) may be one of these vibrations.

The simple vibrational structure of the visible absorption spectrum of *sym*-tetrazine at 77° K is complicated at room temperature by a number of progressions in the dominant frequency of 690—700 cm.$^{-1}$, due to the vibration mode (A), which build on the sequences clustering round the band origin. One such progression, marked (D) in the Figure, is notable in that it includes the high-intensity vibrational bands of the shorter wavelength part of the spectrum of the vapour, and that the intensity maximum occurs at the third member, (D_3), in contrast to the main progression in the mode (A) where the intensity maximum is found in the 0–0 band (Fig.). The origin of the progression (D) appears to be the sequence (D_1), which, lying to the blue side of the 0–0 band, is due to a vibration which has a higher frequency in the excited than the ground state. The intensity maximum of the progression (D) indicates that the turning points of the active ground-state vibration correspond most closely to those of a state excited electronically together with one quantum of the same active vibration and two quanta of the mode (A). The active vibration of the sequence (D_1) is probably an in-plane mode, as otherwise the intensity distributions in the progressions (A) and (D) would be similar. For the mode to be appreciably populated in the ground state at room temperature, the vibration must be of low frequency. It cannot be the mode (A) itself, and the only other in-plane ring vibration of *sym*-tetrazine with a frequency less than 1000 cm.$^{-1}$ is the B_{3g} mode (E), which should have a frequency similar to that of (A), as in benzene [12] and *sym*-triazine [11] (A) and (E) are degenerate.

Experimental

Materials.—*sym*-Tetrazine and its 3 : 6-dimethyl and 3 : 6-dicarboxylic acid derivatives were prepared by the methods of Curtius, Darapsky, and Muller.[1,13] Dideuterotetrazine was prepared by the decarboxylation of the dideuterotetrazine-3 : 6-dicarboxylic acid at 150°. No bands due to C–H vibrations were detected in the infrared spectrum of the compound.

Spectra.—These were measured with a Cary recording spectrophotometer. The spectra of the vapour were obtained in an evacuated 10-cm. cell at the vapour pressure of the solid (*ca.* 1 mm.) at room temperature. The spectrum at liquid-nitrogen temperature was measured with a M/2000-solution of *sym*-tetrazine in a glass composed of a 5 : 1-mixture of *iso*pentane and methyl*cyclo*hexane, purified by Potts's method,[14] the low-temperature cell described by Passerini and Ross [15] being used. The measured frequencies were accurate to within 20 cm.$^{-1}$, and the optical densities to within 2—3%.

The author thanks Professor Sir Christopher Ingold, F.R.S., for the use of the Cary spectrophotometer at University College, London.

Chemistry Department, The University, Exeter. [*Received, August 26th*, 1958.]

[13] Curtius, Darapsky, and Muller, *Ber.*, 1915, **48**, 1614.
[14] Potts, *J. Chem. Phys.*, 1952, **20**, 809.
[15] Passerini and Ross, *J. Sci. Instr.*, 1953, **30**, 274.

249. *The Electronic Spectra of* N*-Heteroaromatic Systems. Part V.* The Rotational Structure of the Vibrationless Band in the* $n \longrightarrow \pi$ *Transition of* sym*-Tetrazine.*

By S. F. Mason.

The 0–0 band in the absorption spectrum of *sym*-tetrazine, at 5515 Å, has been photographed with a 20-ft. Ebert grating spectrograph. The rotational structure observed shows well-defined *P*, *Q*, and *R* branches, with a slight degradation towards the blue end of the spectrum, and in overall appearance it resembles a parallel band of an oblate symmetric top. The electronic transition moment lies perpendicular to the plane of the molecule, and one or both of the moments of inertia about the twofold axes in the molecular plane decrease on excitation. An analysis of the structure based on the symmetric-top approximation gives an average rotational constant for the ground state agreeing satisfactorily with that calculated from the dimensions of *sym*-tetrazine determined by *X*-ray diffraction.

The visible absorption spectrum of *sym*-tetrazine (I) in the vapour consists of a series of narrow bands, which were likened to the lines of atomic spectra by Koenigsberger and Vogt,[1] who were the first to examine the absorption quantitatively. The bands comprise the vibrational structure of an absorption due to the transition of an electron from a lone-pair orbital of the nitrogen atoms to a π-orbital of the ring,[2] and a vibrational analysis has shown [3] that there is little change in the size of the molecule on excitation. It appeared probable, therefore, that the moments of inertia of *sym*-tetrazine would not alter greatly during the transition, so that rotational fine structure might be observed with adequate resolution, despite the relatively large size of the molecule, allowing the absorption to be more precisely characterised. The absorption of *sym*-tetrazine in the region of the 0–0

The rotational fine structure of the 0–0 *vibrational band in the* $n \longrightarrow \pi$ *electronic absorption spectrum of* sym*-tetrazine. The positions of the* P *and the* R *lines are given relative to the iron arc line at* 18,133·583 cm.$^{-1}$.

J	R_J (cm.$^{-1}$)	P_J (cm.$^{-1}$)	J	R_J (cm.$^{-1}$)	P_J (cm.$^{-1}$)	J	R_J (cm.$^{-1}$)	P_J (cm.$^{-1}$)
5	2·568	−2·327	18	8·689	−7·655	31	14·849	—
6	3·061	—	19	9·327	−8·146	32	15·390	−13·734
7	3·476	−3·212	20	9·597	−8·598	33	15·680	−14·080
8	3·978	−3·732	21	10·022	−8·944	34	16·356	−14·407
9	4·461	−4·039	22	10·601	−9·252	35	16·800	−14·984
10	4·895	−4·443	23	11·181	−9·741	36	17·225	−15·407
11	5·368	−4·789	24	11·547	−10·225	37	17·919	−15·946
12	5·812	−5·251	25	12·049	−10·625	38	18·248	−16·350
13	6·295	−5·628	26	12·455	−10·983	39	18·707	−16·696
14	6·807	−6·047	27	13·073	−11·445	40	—	−17·176
15	7·261	−6·482	28	—	−11·976	41	19·677	−17·600
16	7·685	−6·909	29	13·807	−12·445	42	20·314	−17·908
17	8·207	−7·369	30	14·425	−12·830	43	20·855	−18·215

vibrational band [3] at 5515 Å has now been photographed at a resolution of 150,000 with an Ebert grating spectrograph.[4] A microphotometer tracing of the rotational fine structure found in the 0–0 band is given in Fig. 1, the positions of a number of rotational lines observed being recorded in the Table.

* Part IV, preceding paper.

[1] Koenigsberger and Vogt, *Physikal. Z.*, 1913, **14**, 1269.
[2] Part I, *J.*, 1959, 1240.
[3] Part IV, preceding paper.
[4] King, *J. Sci. Instr.*, 1958, **35**, 11.

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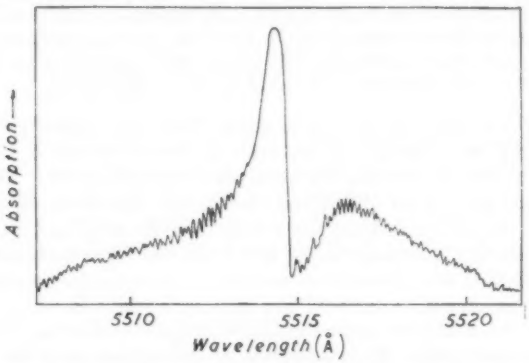
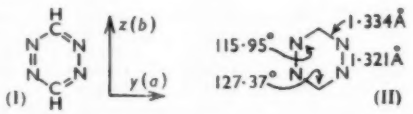
The rotational structure of the vibrationless band in the visible absorption of *sym*-tetrazine shows well-defined P, Q, and R branches, and indicates that the apparent sharpness of the vibrational bands under lower resolution is due to the particularly prominent central Q branch (Fig. 1). A small but distinct degradation of the rotational structure towards the blue region can be observed (Table; Fig. 1), suggesting that the moments of inertia of *sym*-tetrazine are slightly smaller in the excited state than in the ground state. The overall appearance of the rotational-electronic band in the visible absorption of *sym*-tetrazine (Fig. 1) is that of a parallel band of an oblate symmetric top, involving little change in the moments of inertia of the molecule on excitation. For a planar molecule, such a band should consist of simple P, Q, and R branches with almost half of the total intensity of the band in the Q branch.[5]

FIG. 1. *The rotational structure of the* 0—0 *band in the visible absorption spectrum of* sym-*tetrazine.*



sym-Tetrazine is an asymmetric top, the moments of inertia, I_a, I_b, and I_c, calculated from the bond distances and bond angles (II) determined by X-ray diffraction [6] and an assumed C–H bond distance of 1·0 Å, being 1·200, 1·330, and 2·530 × 10^{-38} g. cm.^{2}, respectively, in the ground state. The asymmetry parameter $\kappa = (2B - A - C)/(A - C) \simeq 0{\cdot}80$ in the ground state, A, B, and C being the corresponding rotational constants. Thus *sym*-tetrazine is sufficiently similar to an oblate symmetric top for the parallel-type appearance of the rotational-electronic band to show that the visible absorption of the compound is due to an electronic excitation with the transition moment perpendicular to the plane of the molecule.



(I) (II)

The assignment of the visible absorption of *sym*-tetrazine to the promotion of an electron from a lone-pair orbital of the nitrogen atoms to a π-orbital of the ring [2] requires that the transition should be polarised perpendicular to the molecular plane. The highest occupied (ψ_g) of the lone-pair molecular orbitals, which are formed by the overlap and interaction [2] of the four lone-pair atomic orbitals (ϕ) in *sym*-tetrazine, has the form

$$\psi_g = (\phi_2 - \phi_3 + \phi_5 - \phi_6)/2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

and the lowest unoccupied π-orbital (ψ_e) is, similarly

$$\psi_e = (\theta_2 - \theta_3 + \theta_5 - \theta_6)/2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

[5] Gerhard and Dennison, *Phys. Rev.*, **1933**, **43**, 197.
[6] Bertinotti, Giacomello, and Liquori, *Acta Cryst.*, **1956**, **9**, 510.

where θ is a $2p_x$ atomic orbital. The orbitals, ψ_g and ψ_e, have the symmetries B_{3g} and A_u, respectively, in D_{2h}, axes being taken as in (I), and an electronic transition from ψ_g to ψ_e is allowed ($A_g \longrightarrow B_{3u}$), with a transition moment perpendicular to the molecular plane.

A quantitative estimate of the change in the averaged moments of inertia of *sym*-tetrazine during the $n \longrightarrow \pi$ transition can be obtained from the observed rotational structure, a symmetric-top approximation being used. The energy levels of an oblate symmetric top ($I_a = I_b$, $\kappa = 1$) are given by

$$E(J,K) = BJ(J+1) + (C-B)K^2 \quad . \quad . \quad . \quad . \quad . \quad (3)$$

where J and K are quantum numbers associated with the total angular momentum and with its component along the figure axis, respectively, and where $J \geqslant K$. A slightly asymmetric top has similar energy levels, but all levels with $K > 0$ are split into two components. If the splitting is small, a good approximation to the energy levels is provided by

$$E(J,K) = (A+B)J(J+1)/2 + [C - (A+B)/2]K^2 \quad . \quad . \quad . \quad (4)$$

When the symmetric-top approximation to the energy levels is valid for both the ground and excited states, the allowed changes in the rotational quantum numbers for electronic excitations in which the transition moment is parallel to the quasi-symmetry axis [the x or c axis of (I), perpendicular to the molecular plane] are $\Delta J = 0, \pm 1$, and $\Delta K = 0$. For a particular value of K, a sub-band is obtained with P, Q, and R branches, except for $K = 0$: the Q branch is then missing. Each sub-band can be referred to an origin, which is the hypothetical Q line for $J'' = 0$. The frequencies of the sub-band origins, ν_0, are given by the equation

$$\nu_0 = \nu_{00} + \{[C' - (A'+B')/2] - [C'' - (A''+B'')/2]\}K^2 \quad . \quad . \quad (5)$$

where the primes refer to the excited state and the seconds to the ground state, and ν_{00} is the frequency of the electronic origin of the band.

The complete parallel rotational-electronic band is formed by the superposition of a number of such sub-bands, corresponding to the various K values which occur at the temperature of observation. If the moments of inertia in the ground and the excited state are the same, the sub-bands of different K values coincide, with $\nu_0 = \nu_{00}$ in each case. The whole of the parallel band then appears with a strong line-like Q branch and P and R branches, like a perpendicular band of a linear molecule, though in contrast to the latter, each line consists of a number of components, $(J+1)$ in the R branch and J in the P branch. The general appearance is retained if the changes in the moments of inertia on excitation are small, but the band structure then becomes degraded.

The rotational-electronic band in the $n \longrightarrow \pi$ absorption of *sym*-tetrazine corresponds to the latter case (Fig. 1). A K structure is not evident in the band, though the J structure of the P, Q, and R branches is clear. The average rotational constant $(A+B)/2$ can be obtained for the ground and the excited state from the J structure, by using an approximate treatment based upon the method of combination differences [7] employed in the analysis of the perpendicular bands of linear molecules. If the term in K^2 of eqn. (4) is neglected, it follows from the definition of P and R branches ($\Delta J = -1$ and $+1$, respectively) that,

$$R(J) - P(J) = 2(A'+B')(J+1/2) \quad . \quad . \quad . \quad . \quad . \quad (6)$$

$$R(J-1) - P(J+1) = 2(A''+B'')(J+1/2) \quad . \quad . \quad . \quad . \quad (7)$$

$$R(J-1) + P(J) = 2\nu_{00} + (A'+B'-A''-B'')J^2 \quad . \quad . \quad . \quad (8)$$

where $R(J)$ and $P(J)$ are the frequencies of the R and the P lines, respectively, with a given J value.

[7] Herzberg, "Infrared and Raman Spectra of Polyatomic Molecules," D. Van Nostrand Co., New York, 1945, p. 390.

The J values of the lines in the P and the R branch of the rotational electronic band in the $n \longrightarrow \pi$ absorption of *sym*-tetrazine have been obtained by means of a Fortrat diagram (Fig. 2), and the combination differences (eqns. 6—8) have been plotted against the derived J values (Figs. 3 and 4). Eqns. (6) and (7) give satisfactorily linear relations (Fig. 3), from which the average rotational constants 0·2215 and 0·2234 cm.$^{-1}$ are obtained

FIG. 2. *The Fortrat diagram of the relation between the frequencies of the lines in the* P *and the* R *branches of the rotational-electronic band of* sym*-tetrazine and the rotational quantum number,* J.

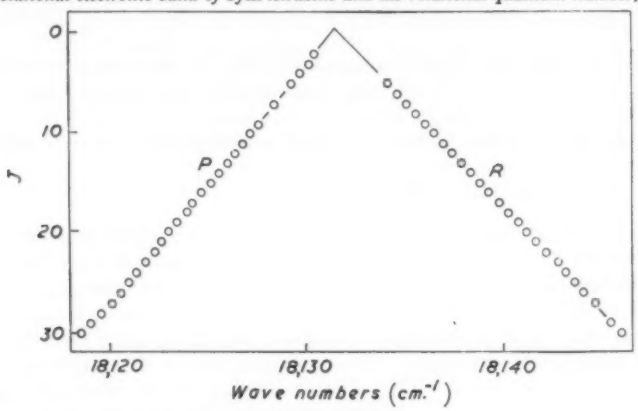


FIG. 3. *The relations between the rotational quantum number,* J, *and the difference in frequency between lines of the* R *and the* P *branches* (A) *with the same* J *value, and* (B) *with the quantum numbers* (J − 1) *and* (J + 1), *respectively (eqns.* 6 *and* 7).

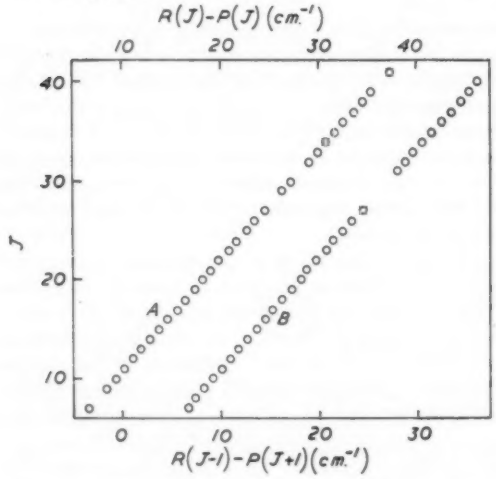
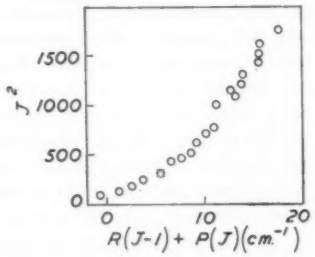


FIG. 4. *The relation between the square of the rotational quantum number,* J^2, *and the sum of the frequencies of lines in the* R *and the* P *branches having the quantum numbers* (J − 1) *and* (J), *respectively (eqn.* 8). *The origin of the frequency scale is placed arbitrarily at* 36,267 *cm.*$^{-1}$.



for the ground and the excited state, respectively. The average ground-state rotational constant $(A + B)/2$ calculated from the bond distances and bond angles measured by X-ray diffraction [6] and an assumed C–H bond distance of 1·0 Å is 0·2219 cm.$^{-1}$, in satisfactory agreement with the spectroscopic value.

Eqn. (8), however, gives a curved plot (Fig. 4), which is due to the approximations employed in the derivation. For J values <about 20, eqn. (8) gives approximately the

same value for the difference between the average rotational constants for the ground and the excited state $(A' + B' - A'' - B'')/2$ as eqns. (6) and (7), but the value falls progressively at higher J values. The larger the J value, the larger are the permitted values of K, and the more important becomes the term in K^2 neglected from eqn. (4). The term enters the expressions for the frequencies of the P and the R lines with the same sign and magnitude (eqn. 4), so that it cancels when the differences of such frequencies are taken (eqns. 6 and 7) but leads to progressive deviations (Fig. 4) when they are summed (eqn. 8).

A notable feature of the present results is the increase in the average rotational constant $(A + B)/2$ of *sym*-tetrazine during the $n \longrightarrow \pi$ transition, demonstrating that one or both of the moments of inertia about the axes in the plane of the molecule (I_a and I_b) decrease on excitation. It is improbable that the decrease is due to a non-planar configuration of the molecule in the excited state, since the fall in the delocalisation energy of the six bonding π-electrons would greatly outweigh the stabilisation of the promoted electron in such a configuration. Benzene remains planar in the excited state of the $A_{1g} \longrightarrow B_{2u}$, $\pi \longrightarrow \pi$ transition [8] though the excitation energy is more than twice as large as that of the $n \longrightarrow \pi$ transition of *sym*-tetrazine.

A planar excited state being assumed, the increase in the average rotational constant $(A + B)/2$ of *sym*-tetrazine is consistent with the increase in the molecular zero-point energy on excitation, which is indicated by the red shift in the 0–0 band when the hydrogen atoms of *sym*-tetrazine are replaced by deuterium.[3] The appearance of sequences to the blue side of the vibrationless band also shows that the frequencies of some of the vibrations of *sym*-tetrazine are increased in the excited state.[3] The implication that the atoms of *sym*-tetrazine become more tightly bound during the $n \longrightarrow \pi$ transition is surprising at first sight, since the excited-state orbital, ψ_e, is more antibonding than the ground-state orbital, ψ_g. The energy of ψ_e lies β_{NN} above that of a $2p$ orbital of nitrogen, the nitrogen–nitrogen resonance integral, β_{NN}, having a value in the region [2,9] of 2—3 ev, whilst ψ_g is antibonding only to the extent of approximately 0·8 ev relative to an atomic s–p hybrid lone-pair orbital of nitrogen.[2] Both ψ_g and ψ_e possess two nodal planes perpendicular to the the molecular plane, passing through the 3 and the 6 position and bisecting the N–N bonds, respectively, so that a weakening and a lengthening of the N–N bonds during the $n \longrightarrow \pi$ transition might be expected, resulting in an increase in the moment of inertia, I_a.

The CNN bond angle in *sym*-tetrazine [6] is 115·95° (II), suggesting that the σ bonds of a nitrogen atom have 30·5% and the lone-pair orbital 39·0% of "*s*" character in the ground state. On the promotion of a lone-pair electron to a π-orbital, the "*s*" character of the "hole" left behind is shared amongst the remaining σ electrons, notably those of the σ bonds. The increase in the "*s*" character of the nitrogen σ bond electrons has the consequences that the CNN bond angle should increase and that the effective atomic radius of the nitrogen atoms should decrease on excitation. In the vibrational structure of the $n \longrightarrow \pi$ absorption of *sym*-tetrazine the main progression is due to the A_g ring-angle bending mode, showing that the CNN angle changes during the transition.[3] An increase in the CNN angle alone does not account for the increased average rotational constant $(A + B)/2$ on excitation, for if the bond lengths of *sym*-tetrazine remain unchanged (II) and all the bond angles become 120° the calculated average rotational constant shows a small fall to the value of 0·2213 cm.$^{-1}$.

If *sym*-tetrazine remains planar in the excited state of the $n \longrightarrow \pi$ transition the observed increase in the average rotational constant is probably due to a small decrease in some of the ring-bond lengths, suggesting that the contraction in the covalent radius of the nitrogen atoms owing to the increased "*s*" character of the σ hybrid bonds on excitation, outweighs the antibonding effect of the promoted electron. The covalent radius of a nitrogen atom may vary considerably with the hybridisation of its σ orbitals.

[8] Garforth, Ingold, and Poole, *J.*, 1948, 508.
[9] Paoloni, *Gazzetta*, 1957, **87**, 313.

In azobenzene,[10] where the CNN angle is 120—123°, depending upon the isomeric and crystallographic form of the molecule, the N–N distance is 1·23 Å, compared with 1·321 Å in *sym*-tetrazine.[6] With the same Coulomb and resonance parameters, the calculated N–N π-bond order is 0·83 in azobenzene [11] and 0·66 in *sym*-tetrazine.[12] It is unlikely that the shorter N–N distance in azobenzene is due entirely to the larger N–N bond order. Part of the shortening is probably derived from the 3—6% larger "*s*" character of the σ bonds in azobenzene, but the relative importance of the two factors cannot be assessed at present.

In the vapour the long-wavelength absorption of the monocyclic azines consists,[2,13,14,15] in general, of a system of narrow bands, comparable to atomic spectral lines. As in the case of *sym*-tetrazine, the absorption is due to a $n \longrightarrow \pi$ transition with a moment perpendicular to the plane of the molecule.[2] The monocyclic azines either are or resemble oblate symmetric tops, and the $n \longrightarrow \pi$ transitions of these compounds should give vibrational bands with a parallel-type rotational structure. If the moments of inertia of the azine do not change greatly during the $n \longrightarrow \pi$ excitation the *Q* lines corresponding to different *K* values superpose, or nearly so, giving a strong line-like *Q* branch, as for *sym*-tetrazine (Fig. 1), thus accounting for the narrowness of the long-wavelength absorption bands. One or both of the moments of inertia about the axes in the plane of *sym*-tetrazine decrease slightly during the $n \longrightarrow \pi$ transition, and in the other azines, which have $n \longrightarrow \pi$ excited states of higher energy, the corresponding moments of inertia probably undergo small increases. The unresolved rotational structure of the narrow vibrational bands in the $n \longrightarrow \pi$ absorption of pyrazine degrades [15] towards the red region, in support of this view, but a few weak and broad vibrational bands, degrading towards the blue region, were also observed.[15]

Experimental

sym-Tetrazine [16] was examined at the vapour pressure of the solid (about 1 mm.) corresponding to room temperature in an evacuated 10-cm. silica cell. Absorption spectra were photographed in the first order of a 20-ft. Ebert grating spectrograph [4] with a high-pressure xenon arc as a light source. Iron-arc comparison spectra were superposed immediately before or after each exposure.

The plate dispersion in the absorption region was approximately 0·59 Å/mm. and the resolving power was 150,000, corresponding to a minimum separation between resolvable lines of approximately 0·04 mm. Microphotometer tracings of the plates were taken with a tenfold magnification, and the positions of the rotational lines were measured in both directions from the tracings and from the plates, a travelling microscope reading to 0·01 mm. being used. The wavelengths of the rotational lines were obtained by interpolation from the wavelengths of the iron-arc reference lines, and they were converted into vacuum wavenumbers (Table).

The author is indebted to Dr. G. W. King for the photographs of the spectrum, and to Dr. H. G. Poole for the microphotometer tracings of the plates.

Chemistry Department, The University, Exeter. [*Received, September 9th*, 1958.]

[10] Lange, Robertson, and Woodward, *Proc. Roy. Soc.*, 1939, *A*, **171**, 398; Hampson and Robertson, *J.*, 1941, 409.
[11] Present work.
[12] Liquori and Vaciago, *Ricerca sci.*, 1956, **26**, 181.
[13] Rush and Sponer, *J. Chem. Phys.*, 1952, **20**, 1847.
[14] Uber, *ibid.*, 1941, **9**, 777.
[15] Ito, Shimada, Kuraishi, and Mizushima, *ibid.*, 1957, **26**, 1508.
[16] Curtius, Darapsky, and Müller, *Ber.*, 1907, **40**, 84.

250. *The Frequencies and Intensities of the* N–H *Stretching Vibrations in Primary Amines. Part II.*[1] *Polycyclic Aromatic Amines.*

By J. J. Elliott and S. F. Mason.

The positions, extinction coefficients, and band half-widths of the symmetric and antisymmetric N–H stretching vibration absorptions of some polycyclic aromatic amines have been measured in the 3 μ region, and approximate values for the force constants and the HNH bond angles have been calculated from the results. These HNH bond angles increases as the π-electron charge density q_r at the exocyclic position of the carbanion corresponding to the amine falls, two relations being observed, one for the unhindered and the other for the *peri*-amines. The intensity of the symmetric stretching vibration band also increases as q_r falls in the series of unhindered amines, but not in the *peri*-series. It is concluded that conjugation between the amino-group and the aromatic nucleus is sterically hindered in the *peri*-amines.

In monocyclic *N*-heteroaromatic amines it has been shown,[1] from the frequencies and the intensities of the N–H stretching vibrations, that the HNH bond angle, the N–H stretching force constant, and the N–H bond dipole gradient increase, relative to the values for aniline, as the lone-pair electrons of the amino-group are increasingly drawn into conjugation with the π-electron system of the nucleus by aza-substitution in the ring. These trends are due to varying hybridisation ratios in the orbitals of the nitrogen atom of the amino-group. As the lone-pair orbital becomes more nearly $2p\pi$, owing to conjugation with the nucleus, the " *s* " character of the N–H bonds increases, so that the HNH angle opens and the N–H bond becomes stronger and more polar, owing to, respectively, the better overlap of the nitrogen and hydrogen orbitals and the enhanced electronegativity of the nitrogen relative to the hydrogen atom. The effect upon the structure of the amino-group in aniline of another type of conjugation, that due to condensed or aromatic rings, has now been investigated by the measurement of the positions and the intensities of the symmetric and the antisymmetric N–H stretching vibration bands in a series of polycyclic aromatic amines. The observed frequencies, maximum extinction coefficients, and intensities are recorded in the Table.

In general, a condensed or aromatic ring is found to have a smaller influence than an aza-substituent upon the positions and the intensities of the N–H stretching vibrations of aniline. A given band has a frequency lying within a range of 25 cm.$^{-1}$ and an intensity which varies by a factor of two in the series of polycyclic aromatic amines (Table), but in the monocyclic amino-azine series the range is 60 cm.$^{-1}$ and the intensity varies by a factor of five.[1] The two series are comparable in that compounds with up to three " substituent," ring nitrogen atoms, or condensed rings, have been investigated. The smaller effect of the condensed ring upon the conjugation of an aromatic amino-group appears to be partly inherent, and partly due to steric factors. In a polycyclic aromatic hydrocarbon the *peri*- and *meso*-positions have a high conjugating capacity, but in those positions the conjugation of a substituent, such as an amino-group, may be sterically hindered.

It may be assumed, as previously,[1] that the two absorption bands in the 3μ region of the infrared spectra of primary amines are due to vibrations in which only the nitrogen and the hydrogen atoms move, and that these atoms vibrate along the N–H bond directions. With these assumptions the HNH bond angle (θ) and the N–H stretching force constant (k) can be calculated from the frequencies of the symmetric (ν_s) and the antisymmetric (ν_a) absorption bands by using the valency force field equations due to Linnett,[2] namely

$$4\pi^2\nu_s^2 = k[1/m_H + (1 + \cos\theta)/m_N] \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

$$4\pi^2\nu_a^2 = k[1/m_H + (1 - \cos\theta)/m_N] \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

[1] The paper, *J.*, 1958, 3619, is regarded as Part I.
[2] Linnett, *Trans. Faraday Soc.*, 1945, **41**, 223.

The positions (ν) *and the intensities* (I) *of the symmetric and antisymmetric* N–H *stretching vibration bands of some polycyclic aromatic amines and* cyclo*hexylamine in carbon tetrachloride. The intensities* (I) *are given as the product of the maximum extinction coefficient* [$E_{max.} = (1/Cl) \log_{10} (T_0/T)\ \nu_{max.}$] *and the band half width. The* N–H *stretching vibration force constants* (k), *the* HNH *bond angle* (θ), *and the* π*-electron charge density at the position of the exocyclic atom in the corresponding carbanion* (q_r).

		Antisymmetric			Symmetric					
	Compound	ν (cm.$^{-1}$)	$E_{max.}$ (l. mole^{-1} cm.$^{-1}$)	I (l. mole^{-1} cm.$^{-2}$)	ν (cm.$^{-1}$)	$E_{max.}$ (l. mole^{-1} cm.$^{-1}$)	I (l. mole^{-1} cm.$^{-2}$)	10^5k [a] (dyne cm.$^{-1}$)	θ [a] (deg.)	q_r [b]
	Unhindered									
1	Aniline	3473	22	960	3390	24	760	6·52	111·1	1·572
2	*m*-Aminodiphenyl	3476	23	970	3391	27	820	6·53	111·9	1·572
3	*p*-Aminodiphenyl	3480	22	960	3393	29	930	6·54	112·1	1·516
4	2-Aminofluorene	3475	22	980	3389	31	960	6·52	111·9	1·516
5	2-Naphthylamine	3477	24	970	3392	31	920	6·53	111·6	1·529
6	2-Phenanthrylamine	3477	26	1020	3394	39	1080	6·54	111·4	1·543
7	3-Phenanthrylamine	3480	27	1070	3393	40	1160	6·54	112·4	1·510
8	2-Anthrylamine	3480	25	930	3392	46	1220	6·54	112·7	1·471
	Hindered									
9	*o*-Aminodiphenyl	3475	27	1260	3385	24	800	6·52	113·0	1·516
	peri									
10	1-Naphthylamine	3470	21	810	3391	22	630	6·52	110·3	1·450
11	1-Phenanthrylamine	3471	23	850	3393	25	690	6·52	110·0	1·463
12	9-Phenanthrylamine	3464	22	800	3386	27	720	6·50	109·8	1·446
13	1-Anthrylamine	3468	21	810	3387	23	600	6·51	110·6	1·381
14	2-Aminochrysene	3469	18	750	3390	26	760	6·52	110·1	1·410
15	3-Aminopyrene	3482	24	960	3400	34	1080	6·56	110·8	1·364
	meso									
16	9-Anthrylamine	3489	19	750	3412	22	690	6·60	109·4	1·286
	Saturated									
17	*cyclo*Hexylamine	3375	3·3	155	3311	2·1	98	6·19	107·1	—

[a] Calculated by equations (1) and (2). [b] Calculated by the method of ref. (3).

where m_H and m_N are the mass of the hydrogen and the nitrogen atom, respectively. The bond angles and force constants of the polycyclic aromatic amines, calculated by means of equations (1) and (2), are recorded in the Table. The HNH bond angle in the *meso*- and the *peri*-amines is less than that of aniline, and in the series as a whole the angle varies only from 109 to 113° (Table), compared with the range 111—119° observed in the amino-azine series.[1]

A measure of the conjugating capacity of a given position in a polycyclic aromatic nucleus is afforded by the π-electron charge density, q_r, at the exocyclic position in the corresponding carbanion, *e.g.* the benzyl anion in the case of benzene. The greater the conjugation at the position of the exocyclic group, the more charge is drawn into the nucleus and the smaller the value of q_r. The charge densities, q_r, are readily found by Longuet-Higgins's method,[3] and the values for the carbanions analogous to the amines studied are recorded in the Table.

The lone-pair charge density, q_N, on the nitrogen atom of an aromatic amine is related to q_r by the expression

$$q_N = q_r + \pi_{r,r}\Delta\alpha_N \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

where $\pi_{r,r}$ is the self-polarisability of the exocyclic atom in the corresponding carbanion, and $\Delta\alpha_N$ is the increment in the Coulomb integral of nitrogen relative to carbon. Values of $\pi_{r,r}$ have been derived[4] for the benzyl anion,[5] the 1- and 2-naphthylmethyl,[6] and the

[3] Longuet-Higgins, *J. Chem. Phys.*, 1950, **18**, 265.
[4] Coulson and Longuet-Higgins, *Proc. Roy. Soc.*, 1947, *A*, **191**, 39.
[5] Jaffe, *J. Amer. Chem. Soc.*, 1954, **76**, 3527.
[6] Present work.

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9-anthrylmethyl ions,[6] namely, 0·412, 0·590, 0·501, and 0·724 β^{-1}, respectively, where β is the carbon–carbon resonance integral. These values span the range of conjugating capacities studied in the present series, and they are smoothly related to the corresponding value of q_r (Table). The relation is probably general in the present series, so that q_r affords a semi-quantitative measure of q_N.

In aliphatic amines the HNH bond angle is ~107° (Table), the " *s* " character of the nitrogen bonding orbitals being less than sp^3 whilst that of the lone-pair orbital is greater. In aromatic amines the lone-pair orbital must assume a larger " *p* " character in order to conjugate with the π-electron system of the nucleus, and compensating hybridisation ratio changes in the nitrogen bonding orbitals result in a larger HNH bond angle. The angles

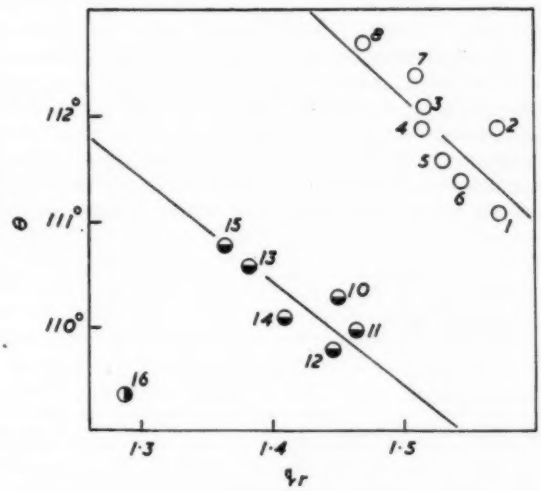

FIG. 1. *The relations between the* HNH *bond angle, θ, of some polycyclic aromatic amines and the charge density, q_r, at the exocyclic position of the corresponding carbanion.* ◑ meso, ◑ peri, *and* ○ *unhindered amines. The numbers refer to the compounds listed in the Table.*

should increase in the series of polycyclic aromatic amines the more the lone-pair electrons of the amino-group are delocalised over the aromatic nucleus, that is, the smaller the value of q_N, or its measure, q_r. It is found (Table; Fig. 1) that the angles increase as the charge density, q_r, falls, but two distinct relations are observed, one for the unhindered and the other for the *peri*-amines, whilst the point for the *meso*-compound, 9-anthrylamine, lies off both correlations.

The HNH bond angles (θ) of the *meso*- and *peri*-amines are smaller than expected from the magnitudes of the corresponding charge densities, q_r, and the observed relation for the unhindered amines between these quantities (Fig. 1). The reduction appears to be due, partly to the compression of the HNH angle, and partly to the inhibition of resonance between the lone-pair electrons and the aromatic nucleus. The repulsion between a N–H and a *peri* C–H group results in the displacement of the centre of the 1*s* hydrogen orbital from the symmetry axis of the nitrogen bonding orbital, giving a " bent " bond, and in the twist of the amino-group so that the nodal plane of the *p*-component of the lone-pair orbital no longer coincides with the plane of the aromatic nucleus, reducing the interaction with the π-electron system.

The calculated N–H stretching force constants of the polycyclic aromatic amines allow these effects to be distinguished. In general, the N–H stretching force constant increases with the " *s* " character of the N–H bond, since the 2*s* orbital of nitrogen affords better overlap than does the 2*p* with the 1*s* orbital of hydrogen at an internuclear distance of ~1 Å and forms stronger bonds.[1] In the series of aromatic amines, 9-anthrylamine has

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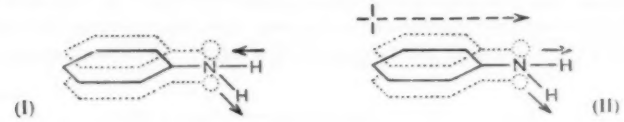
the largest force constant but the smallest HNH bond angle (Table), suggesting that the N–H bonds have the large " *s* " character appropriate to the high conjugating capacity of the 9-anthryl position and that the HNH angle is compressed. On the other hand, 9-phenanthrylamine has a smaller force constant and HNH bond angle than any of the unhindered amines (Table), indicating that, although the conjugating capacity of the 9-phenanthryl position is substantial, the delocalisation of the amine lone-pair electrons over the aromatic nucleus is partly inhibited.



The intensities of the N–H stretching vibration absorption bands in the series of polycyclic aromatic amines suggest that a change in the conjugation of the lone-pair electrons with the aromatic nucleus during the transition from the ground to the vibrationally excited state is also partly inhibited in the *meso*- and *peri*-amines. The intensity of an absorption band in the infrared region is proportional to the square of the change of dipole moment with the vibration. To a good approximation,[1] only the change of the N–H bond moment with bond length contributes to the transition moment of the antisymmetric

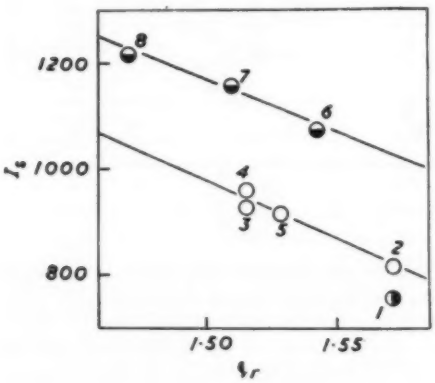


FIG. 2. *The relations between the intensity of the symmetric* N–H *stretching vibration absorption band of some unhindered polycyclic aromatic amines,* I_s, *and the charge density at the exocyclic position of the corresponding carbanion,* q_r. *The numbers refer to the compounds listed in the Table.* ◑ *Mono-,* ○ *di-, and* ◒ *tricyclic amines.*

stretching vibration in primary amines, but there is an additional contribution from the variation of the atomic dipole of the lone-pair electrons to that of the symmetric stretching vibration.[7]

When a N–H bond is stretched the " *s* " character of the nitrogen hybrid orbital falls, as the 2*p* orbital of nitrogen affords better overlap than does the 2*s* with the 1*s* orbital of hydrogen at large internuclear distances. In the antisymmetric stretching vibration (I) any change of hybridisation in one N–H bond is largely compensated by a converse change in the other, and the intensity of the corresponding absorption band should depend mainly upon the N–H bond dipole gradient and the HNH bond angle.[1] However, in the symmetric stretching vibration (II) both N–H bonds, on stretching, increase in " *p* " character, and compensating hybridisation changes must occur in the other nitrogen orbitals, notably, in the lone-pair orbital which undergoes an increase in " *s* " character.

In the ground state of aromatic amines the lone-pair electrons are delocalised over the

[7] Orville-Thomas, Parsons, and Ogden, *J.*, 1958, 1047.

nucleus, and when the lone-pair orbital assumes an increased " *s* " character during the symmetric stretching vibration these electrons are withdrawn from the aromatic system and localised upon the nitrogen atom, since the 2*s* orbital of nitrogen, with even symmetry, cannot combine with the π orbitals of the nucleus, which have odd symmetry with respect to the molecular plane. Accordingly, the π-electron component of the permanent dipole moment of aromatic amines varies in phase with the symmetric stretching vibration of the amino-group, and the variation contributes to the intensity of the corresponding infrared absorption band. The contribution should increase the larger the aromatic nucleus, and the greater the conjugation between the lone-pair electrons of the amino-group and the nucleus, that is, the smaller the charge density, q_r.

The intensity of the symmetric stretching vibration absorption band, I_s, in the unhindered polycyclic aromatic amines increases (Table, Fig. 2) with the number of aromatic rings in the molecule, and increases as the charge density, q_r, falls. The relation between I_s and q_r for the tricyclic amines (Fig. 2) lies above and parallel to the corresponding relation for the bicyclic amines (Fig. 2), which in turn lies above the point for aniline. In the series of *meso*- and *peri*-amines, except for 3-aminopyrene, the intensities of the symmetric stretching vibration bands do not vary widely, and they are smaller than those of the corresponding bands in the series of unhindered amines (Table), suggesting not only that conjugation between the lone-pair electrons of the amino-group and the aromatic nucleus is sterically hindered in the ground state of the *meso*- and *peri*-amines, but also that changes of conjugation with the symmetric stretching vibration are likewise hindered.

The intensities of the antisymmetric stretching vibration bands do not cover a wide range in either of the series of amines, although the antisymmetric bands of the *meso*- and *peri*-amines, in general, are somewhat less intense than those of the unhindered amines (Table). It is probable that the N–H bond dipole gradient does not vary widely in either series, and is reduced by steric hindrance between a N–H and a *peri*-C–H group, since the smaller HNH bond angles of the *meso*- and *peri*-amines do not account entirely for the smaller intensities of their antisymmetric stretching vibration bands.

The intensities of the antisymmetric and more particularly the symmetric stretching vibration bands of 3-aminopyrene are greater than those of any other *peri*-amine, and they fall, in fact, within the respective ranges typical of the unhindered amines (Table). In a parallel study of the basicities of the present series of amines in 50% ethanol–water, it has been found [8] that the entropy of ionisation of the conjugate acid of 3-aminopyrene is larger than that of any other *peri*-amine and is typical of an unhindered amine. The reduction of steric hindrance in the 3-position of pyrene is not peculiar to the amino-group, for the reduced rate of the S_N1 reactions of the *peri*-arylmethyl chlorides, due to steric hindrance in the carbonium ion transition state,[9,10] is not observed in the case of 3-pyrenylmethyl chloride.[10]

Steric hindrance between a C–H bond and a methyl or amino-group in the *peri*-positions of pyrene may be small or absent because of the long nuclear carbon–carbon bonds separating these positions. In pyrene [11] the $C_{(2)}$–$C_{(2a)}$ and the $C_{(2a)}$–$C_{(3)}$ bonds have lengths of 1·45 and 1·42 Å, respectively, whilst in anthracene [12] the $C_{(1)}$–$C_{(1a)}$ and the $C_{(1)}$–C_9 bonds are 1·418 and 1·398 Å long, respectively, and the corresponding bonds in naphthalene have lengths [12] of 1·425 Å. The angle between the carbon–carbon bonds separating the *peri*-positions in pyrene is uncertain, but it is unlikely to be so small that those positions are as close together in pyrene as they are in naphthalene or anthracene.

The observed frequencies and intensities of the N–H stretching vibrations and the calculated force constants of the *peri*-amines are much more similar to those of the unhindered aromatic amines than to those of *cyclo*hexylamine (Table), suggesting that the

[8] Unpublished result.
[9] Dewar and Sampson, *J.*, 1956, 2789; 1957, 2946, 2952.
[10] Fierens, Hannaert, Rysselberge, and Martin, *Helv. Chim. Acta*, 1955, **38**, 2009.
[11] Robertson and White, *J.*, 1947, 358.
[12] Ahmed and Cruickshank, *Acta Cryst.*, 1952, **5**, 852.

steric inhibition of conjugation between the amino-group and the nucleus of the *peri*-amines is not large. The differences between the positions and the intensities of the N–H stretching vibrations of aliphatic and aromatic amines may be due in part to the attachment of the amino-group to a sp^3 and a sp^2 carbon atom in the former and the latter, respectively, but the delocalisation of the lone-pair electrons of the amino-group over the nucleus of the aromatic amines is probably the more important factor.

Experimental

Materials.—*m*-Aminodiphenyl was obtained by the reduction [13] of *m*-nitrodiphenyl.[14] 1- and 2-Aminoanthracene were prepared from the corresponding anthraquinones,[15,16] and the 9-isomer by the reduction [17] of 9-nitroanthracene.[18] 1-, 2-, and 3-Aminophenanthrene were made by the method of Bachmann and Boatner [19] from 1-benzoyl- [20] and 2- and 3-acetyl-phenanthrene,[19] and the 9-isomer was prepared according to Bergstrom and Hornig's directions.[21] The remaining compounds were commercial specimens. Each amine was redistilled or resublimed at 0·2 mm. until it had the b. p. or m. p. recorded in the literature.

Infrared spectra.—These were measured with a Mervyn N.P.L. grating spectrophotometer with use of a *F*-centre filter for the 3 μ region. The effective slit width was about 10 cm.$^{-1}$. The aromatic amines were examined at concentrations in the range M/1000 to M/250, and *cyclo*hexylamine at M/50, a cell 5 cm. in length being used. The intensities were reproducible to within about 5% and the frequencies to within 2 cm.$^{-1}$, though the intensities diverge by up to 20% and the frequencies up to 8 cm.$^{-1}$, from the corresponding quantities for the same amines measured with a prism instrument.[1] The intensities are recorded in the Table as the product of the maximum molar extinction coefficient and the width of the absorption band at half the maximum extinction. The correction factor [22] of $\pi/2$ used previously [1] was not employed since only relative intensities were required in the present work.

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Chemistry Department, The University, Exeter. [*Received, September 9th*, 1958.]

[13] Balcom and Furst, *J. Amer. Chem. Soc.*, 1953, **75**, 4334.
[14] Elkes, Haworth, and Hey, *J.*, 1940, 1285.
[15] Fierz-David, Blangey, and Streiff, *Helv. Chim. Acta*, 1946, **29**, 1718.
[16] Ruggli and Henzi, *ibid.*, 1930, **13**, 429.
[17] Meisenheimer, *Ber.*, 1900, **33**, 3547.
[18] Dimroth, *Ber.*, 1901, **34**, 221.
[19] Bachmann and Boatner, *J. Amer. Chem. Soc.*, 1936, **58**, 2097.
[20] Gore, *J. Org. Chem.*, 1957, **22**, 135.
[21] Bergstrom and Hornig, *ibid.*, 1946, **11**, 334.
[22] Ramsey, *J. Amer. Chem. Soc.*, 1952, **74**, 72.

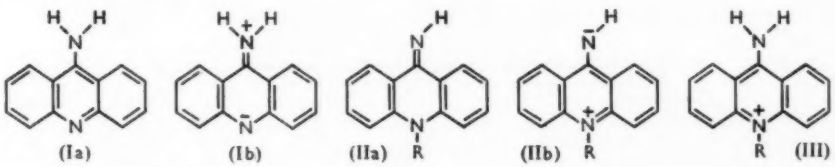
XUM

251. *The Tautomerism of* N-*Heteroaromatic Amines.*

By S. F. Mason.

The frequencies, extinction coefficients, and band half-widths of the N–H stretching vibration bands of some *N*-heteroaromatic imines, and primary and secondary amines, in dilute carbon tetrachloride solution have been measured in the 3 μ region. The amines give absorption bands lying at higher frequencies by 100—200 cm.$^{-1}$ and some five to ten times more intense than those of the imines, differences which are ascribed to the larger "*s*" character of the N–H bonds in the former compounds. The spectral distinctions are used to show that most of the tetracyclic and all of the tricyclic amines examined, including 5-aminoacridine, exist predominantly as the amino-tautomer, although 5-amino-2 : 3-benzacridine assumes largely the imino-form. The ionisation constant and ultraviolet evidence are reviewed and are shown to support an amino-structure for 5-aminoacridine. The present conclusions are shown to be in accord with the expectations of molecular-orbital theory.

It has been shown by various physical methods [1-7] that the mono- and di-cyclic *N*-heteroaromatic amines exist predominantly in the amino- and not the tautomeric imino-form. In dilute chloroform or carbon tetrachloride solution such amines give two absorption bands in the 3350—3550 cm.$^{-1}$ region [1-5] and another in the 1600—1650 cm.$^{-1}$ region,[1-4] due to the symmetric and the antisymmetric stretching vibrations and the internal deformation mode of the primary amino-group respectively, these bands being readily identified by the deuteration of the amino-group.[4] The ultraviolet spectra of these amines, in general, resemble more closely those of the dimethylamino-analogues with fixed amino-forms than those of the corresponding nuclear *N*-methyl derivatives with fixed imine structures,[4,6,7] and the ionisation constants of the amines and their nuclear and exocyclic *N*-methyl derivatives show [4,7] that the amino- predominates over the imino-form by a factor of 10^3—10^6. The tautomerism of *N*-heteroaromatic amines has been investigated also by dipole moment measurements, but the results were inconclusive.[3,7,9]



(Ia) (Ib) (IIa) (IIb) (III)

The structure of the tricyclic amines, notably 5-aminoacridine, has remained uncertain, however. Comparing the ultraviolet spectra of 9-aminoanthracene and 5-aminoacridine, Craig and Short concluded that [10] the latter amine had the amino-structure (I), and Short subsequently found [3] bands at 3435 and 3525 cm.$^{-1}$ in the infrared spectrum of 5-aminoacridine in chloroform, which were assigned respectively to the symmetric and the antisymmetric stretching vibration of the primary amino-group. Working with carbon tetrachloride solutions of 5-aminoacridine, Karyakin and Schablja observed [11] the same

[1] Angyal and Werner, *J.*, 1952, 2911.
[2] Goulden, *J.*, 1952, 2939.
[3] Short, *J.*, 1952, 4584.
[4] Brown, Hoerger, and Mason, *J.*, 1955, 4035.
[5] Osborn, Schofield, and Short, *J.*, 1956, 4191.
[6] Anderson and Seeger, *J. Amer. Chem. Soc.*, 1949, **71**, 340.
[7] Angyal and Angyal, *J.*, 1952, 1461.
[8] Leis and Curran, *J. Amer. Chem. Soc.*, 1945, **67**, 79.
[9] Pushkarev and Kokoshko, *Doklady Akad. Nauk S.S.S.R.*, 1953, **93**, 77.
[10] Craig and Short, *J.*, 1945, 419.
[11] Karyakin and Schablja, *Doklady Akad. Nauk S.S.S.R.*, 1957, **116**, 969.

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TABLE 1.

The positions (ν; cm.$^{-1}$) and the intensities (I; l. mole^{-1} cm.$^{-2}$) of the symmetric and antisymmetric N–H stretching vibration bands of some polycyclic *N*-heteroaromatic primary amines in chloroform and carbon tetrachloride. The intensities (I) are given as the product of the maximum extinction coefficient (l. mole^{-1} cm.$^{-1}$), $E_{max.} = (1/Cl) \log_{10} (T_0/T)\nu_{max.}$, and the band half-width. The H–N–H bond angle ($\theta°$), and the charge densities at the positions of the nuclear (q_n) and the exocyclic (q_x) nitrogen atom in the corresponding carbanion, are also given. Values in italics refer to chloroform solution.

	Antisymmetric			Symmetric					
Compound	ν	$E_{max.}$	I	ν	$E_{max.}$	I	θ [a]	q_n [b]	q_x [b]
Acridine									
1-NH_2	3498	55	1650	3387	58	1330	118·5°	1·000	1·381
2-NH_2	3497	46	1470	3405	102	2240	113·5	1·118	1·471
3-NH_2	3488	31	990	3400	82	1800	112·4	1·000	1·471
4-NH_2	3477	24	940	3395	37	920	110·8	1·095	1·381
5-NH_2	*3527*	*40*	*1280*	*3436*	*97*	*2520*	113·2	1·286	1·286
5-NH_2-1-Me	3523	42	1140	3433	83	1910	112·9	1·286	1·286
Phenanthridine									
6-NH_2	3499	37	1180	3408	85	1870	113·2	1·082	1·510
9-NH_2	3513	46	1420	3409	80	1680	116·5	1·286	1·446
2-NH_2-9Me	3491	23	810	3403	54	1240	112·4	1·022	1·544
Benzoquinoline									
4′-NH_2-5 : 6-	3482	25	850	3401	40	920	110·5	1·019	1·464
2-NH_2-4-Me-5 : 6-	3512	50	1600	3410	96	2210	116·0	1·195	1·544
3-NH_2-6 : 7-	3484	31	960	3398	71	1630	111·8	1·000	1·471
4-NH_2-6 : 7-	3500	40	1080	3415	72	1660	111·6	1·214	1·381
4-NH_2-7 : 8-	3509	43	1160	3419	77	1620	112·9	1·167	1·464
6-NH_2-7 : 8-	3474	25	850	3393	38	870	110·5	1·000	1·446
1′-NH_2-7 : 8-	3475	25	850	3395	39	970	110·3	1·000	1·464
Benzacridine									
5-NH_2-1 : 2-	3523	40	1120	3432	92	2025	113·2	1·231	1·314
7-NH_2-1 : 2-	3490	28	896	3401	72	1655	112·7	1·000	1·495
8-NH_2-1 : 2-	3497	30	870	3405	83	1825	113·5	1·088	1·480
7-NH_2-2 : 3-	3490	29	956	3401	81	1780	112·7	1·000	1·417
5-NH_2-3 : 4-	3488	42	1050	3405	54	1135	111·0	1·250	1·340
7-NH_2-3 : 4-	3492	25	750	3402	68	1495	113·0	1·000	1·480
8-NH_2-3 : 4-	3498	30	840	3406	88	1850	113·5	1·091	1·495

[a] Calculated by the method of ref. (20). [b] Calculated by the method of ref. 21.

TABLE 2. *N-Heteroaromatic imines and secondary amines (for details see Table* 1).

Compound	ν	$E_{max.}$	I	q_n [b]	q_x
1-Ethyl-1 : 2-dihydro-2-iminopyridine	3325	9·3	240	1·143	1·571
1-Ethyl-1 : 4-dihydro-4-iminopyridine	3278	~10 [a]	~250 [a]	1·143	1·571
5-Imino-10-methylacridan	3294	6·8	170	1·286	1·286
5-Methylaminoacridine	3443 3463	24 22	1080	1·286	1·286
Acridan	3434	45	1350	—	—
5-Amino-2 : 3-benzacridine	3448	49	1420	1·300	1·208
	3298	7·4	180		

[a] Some decomposition observed. [b] Calculated by the method of ref. 21.

bands at 3440 and 3520 cm.$^{-1}$ and assigned them respectively to the stretching vibrations of the nuclear and the exocyclic N–H groups of the imine structure (II; R = H) which had been proposed earlier [12] from a study of the spectrum of the amine in the overtone region. Similarly Acheson and his co-workers concluded [13] from a comparison of the ultraviolet spectra of 5-imino-10-methylacridan and 5-amino- and 5-dimethylaminoacridine that the imine form (II; R = H) was predominant in methanol or ethyl acetate solution, whilst Sukhomlinov, from the same data and additional spectral comparisons, considered [14] the amine structure (I) to the the main tautomer under these conditions.

[12] Karyakin, Grigorovski, and Yaroslavskii, *Doklady Akad. Nauk S.S.S.R.*, 1949, **67**, 679.
[13] Acheson, Burstall, Jefford, and Sansom, *J.*, 1954, 3742.
[14] Sukhomlinov, *Zhur. obshchei Khim.*, 1958, **28**, 1038.

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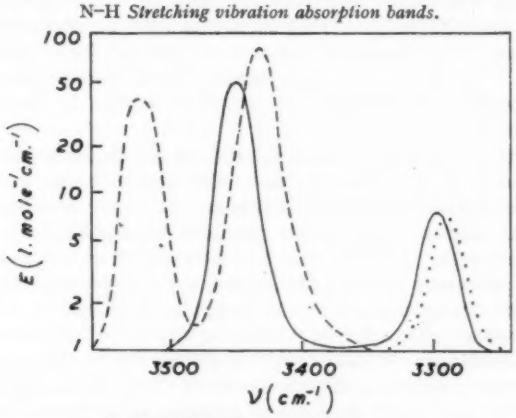
In the case of *peri*- and *meso*-amines the investigation of tautomerism by comparing the electronic spectra of an amine and its *N*-methyl derivatives is complicated by the greater steric hindrance to conjugation between the exocyclic nitrogen atom and the aromatic nucleus in the dimethylamino-compound. There is some steric hindrance to conjugation in the *peri*- and *meso*-amines themselves, as is shown by the reduced H–N–H bond angle,[15] and in the corresponding dimethylamino-derivatives the hindrance must be substantial, giving rise to spectral differences independently of any tautomerism. Thus the ultraviolet spectra of the cationic forms of 9-amino- and 9-methylamino-phenanthridine and 9 : 10-dihydro-9-imino-10-methylphenanthridine are similar, but they differ somewhat from that of the cationic form of 9-dimethylaminophenanthridine,[16] a difference which is due to steric hindrance and not tautomerism, as the amino- and imino-form of an *N*-heteroaromatic amine (*e.g.*, I and II; R = H) give a common cation (*e.g.*, III; R = H).

Steric factors do not limit the study of the tautomerism of *N*-heteroaromatic amines by infrared spectroscopy to the same degree, absorption bands due to the vibrations of N–H groups, which may be similarly hindered in different compounds, being compared

N–H *Stretching vibration absorption bands.*



– – – – – 5-Aminoacridine in chloroform.
———— 5-Amino-2 : 3-benzacridine in carbon tetrachloride.
. . . . . 5-Imino-10-methylacridan in carbon tetrachloride.

directly in this method. Hitherto, only the positions of the infrared bands due to N–H vibrations have been used in the investigation of amine tautomerism,[1-5] although the intensities of such bands also indicate the structure of the absorbing group, as the N–H stretching vibration band intensities cover a range [17] of 10^2, the intensity increasing with the " *s* " character of the N–H bond.[18] In order to obtain further information concerning imine–amine tautomerism, the frequencies, extinction coefficients, and band half-widths of the absorption bands due to the N–H stretching vibrations of a number of tri- and tetra-cyclic *N*-heteroaromatic primary and secondary amines and imines have now been measured in carbon tetrachloride (Tables 1 and 2).

A marked distinction is observed between the spectral characteristics of the absorption bands due to the imine and the amine N–H stretching vibration (Tables 1 and 2, Figure). The imines absorb relatively weakly near 3300 cm.$^{-1}$, whilst the amines give bands five to ten times as intense at frequencies higher by 100—200 cm.$^{-1}$ (Tables 1 and 2). The contrasting spectral properties arise mainly from the different hybridisation ratio in the N–H bond of the two clases of compound. The imine group is isoelectronic with the amide

[15] Elliott and Mason, preceding paper.
[16] Reese, *J.*, 1958, 895.
[17] Russell and Thompson, *J.*, 1955, 483.
[18] Mason, *J.*, 1958, 3619.

anion in one (*e.g.*, IIb) of the two main resonance forms of an *N*-heteroaromatic imine, whilst the N–H group in one (*e.g.*, Ib) of the two principal canonical structures in the corresponding amine is akin to that of pyrrole. The N–H stretching bands of the amide ion lie [19] at 3261 and 3315 cm.$^{-1}$, their intensities being a little smaller than those of the *N*-heteroaromatic imines. The H–N–H bond angle in the amide ion is [19] 104·1°, showing that the low frequencies and the weak intensities of the N–H stretching bands, implying weak N–H bonds of low polarity, are connected with the small " *s* " character of the nitrogen bonding orbitals. The weakness and the low frequency of the imine N–H stretching vibration absorption are probably due to the same cause, as the nitrogen lone-pair orbital which is not in conjugation with the aromatic nucleus may be expected to have a particularly large " *s* " character.

The H–N–H bond angles of the tri- and tetra-cyclic *N*-heteroaromatic amines may be obtained from the frequencies of the symmetric and antisymmetric N–H stretching vibration bands by use of Linnett's valency-force field equations,[20] on the assumption that only the nitrogen and hydrogen atoms of the amino-group move, and that they move along the N–H bond directions, during these vibrations. The calculated H–N–H bond angles (θ) are recorded in Table 1, and they show that the " *s* " character of the N–H bonds of the amines is large, lying, in general, between sp^2 and sp^3. The higher frequencies and intensities of the N–H stretching vibration bands of the *N*-heteroaromatic amines may be ascribed to the larger " *s* " character of the N–H bonds, in conformity with other investigations.[15,18]

The " *s* " character of the N–H bonds in an aromatic amine is determined in part by the hybridisation ratios of the other orbitals of the nitrogen atom, notably, the lone-pair orbital. As the conjugation between the amino-group and the aromatic nucleus increases, the lone-pair orbital becomes more nearly $2p\pi$, and consequently the " *s* " character of the N–H bonds increases. Further, the lone-pair electrons become more completely delocalised over the aromatic nucleus, the smaller is the π-electron charge density on the nitrogen atom. The charge density at the exocyclic atom (q_x) of the carbanion corresponding to the amine provides a semi-quantitative measure of this effect. In a polycyclic *N*-heteroaromatic amine there is additional conjugation due to the polarizing effect of the nuclear nitrogen atom upon the lone-pair electrons of the amino-group (*e.g.*, Ib). The charge density at the position of the nuclear nitrogen atom (q_n) in the carbanion corresponding to the amine affords a semi-quantitative measure of the polarization effect since, in general, the mutual polarizability of a nuclear and the exocyclic atom in a given arylmethyl carbanion increases with the charge density at the nuclear position (q_n). Values of q_x and q_n for the carbanions corresponding to the amines and imines studied, calculated by Longuet-Higgins's method,[21] are recorded in Tables 1 and 2.

In general, the H–N–H bond angle, and thus the " *s* " character of the N–H bonds, becomes larger in the series of polycyclic *N*-heteroaromatic amines as q_n increases and q_x decreases (Table 1), though the trend is overlaid by steric and hydrogen-bonding effects. Comparable pairs of amines free from such effects show, however, the increase of θ with q_n (compounds 2 and 3, 18 and 23, 19 and 22, Table 1). Intramolecular hydrogen-bonding opens up the H–N–H bond angle, *peri*-bonding (compound 1) being more effective in this respect than *ortho*-bonding [18] (compounds 8 and 11). Steric hindrance between the amino-group and *peri*- or *meso*-C–H groups reduces the H–N–H bond angle (cf. compounds 3 and 4, 2 and 6, 12 and 13, 17 and 19), both by the direct compression of the angle and by the partial inhibition of conjugation between the amino-group and the nucleus.[15] However, the H–N–H bond angle suggests that the delocalisation of the lone-pair electrons of the amino-group over the aromatic nucleus remains substantial even in the grossly hindered 5-amino-3 : 4-benzacridine (IV).

[19] Mason, *J. Phys. Chem.*, 1957, **61**, 384.
[20] Linnett, *Trans. Faraday Soc.*, 1945, **41**, 223.
[21] Longuet-Higgins, *J. Chem. Phys.*, 1950, **18**, 265.

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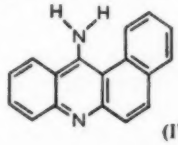
The observed intensities of the N–H stretching vibration bands give further information concerning the structure of the amino-group in the polycyclic *N*-heteroaromatic amines. The intensity of an absorption band in the infrared region is proportional to the square of the change of dipole moment with the vibration responsible for the absorption. To a good approximation,[18] only the change of the N–H bond moment with bond length contributes to the transition moment of the antisymmetric stretching vibration absorption in aromatic primary amines, but there is an additional contribution from the variation in the π-electron component of the permanent dipole of the amine to that of the symmetric stretching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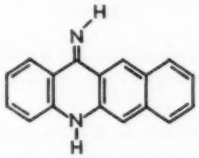
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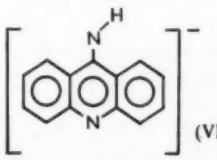
(VI)

vibration.[15] Accordingly, the intensity of the antisymmetric stretching vibration band of the polycyclic *N*-heteroaromatic amine should increase with the " *s* " character of the N–H bonds,[18] whilst that of the symmetric bands should show the additional effect of the variation of conjugation with the vibration.[15]

It is found (Table 1) that the intensities of the antisymmetric stretching vibration bands of the amines studied increase with the H–N–H bond angle, as expected, apart from the *meso*-amines (compounds 5, 6, 17, and 21) where the intensity is large in relation to the angle, suggesting that the angle is sterically compressed.[15] The intensities of the symmetric stretching vibration bands vary more widely (Table 1), indicating that they depend on factors other than the N–H bond dipole gradient. Comparable pairs of unhindered amines show that the intensity of the symmetric band is larger the greater the conjugation between the nitrogen atoms of the nucleus and the amino-group (compounds 2 and 3, 18 and 23, 19 and 22, Table 1). Steric hindrance appears partly to inhibit the variation of conjugation with the symmetric vibration (cf. compounds 3 and 4, 2 and 6, 12 and 13) in the *peri*- and *meso*-amines, and perhaps to suppress the variation entirely in the grossly hindered 5-amino-3 : 4-benzacridine (IV) which has a symmetric band not much more than half as intense as those of the other *meso*-amines (compounds 5, 6, and 17). The N–H stretching vibration band of 5-methylaminoacridine, which has a double peak, is less intense than either of those of 5-aminoacridine (Tables 1 and 2), owing to the greater hindrance introduced with the methyl group. The double peak probably arises from the two conformations of 5-methylaminoacridine, one with the methyl group and the hydrogen atom of the MeNH group on the opposite sides of the plane of the acridine ring, and the other with the methyl group and hydrogen atom on the same side, though it is possible that the two bands are due to the two tautomeric forms.

The characteristics of the infrared absorption bands studied show that all of the tricyclic *N*-heteroaromatic amines, including 5-aminoacridine, and most of the tetracyclic compounds, exist predominantly in the amino-form (*e.g.*, I) in carbon tetrachloride solution. Even in the most hindered amine studied (IV) and in the amines which are both weakly conjugated and partially hindered (compounds 15 and 16) the N–H stretching vibration bands are some five times as intense and 100—200 cm.$^{-1}$ higher in frequency than those of the *N*-heteroaromatic imines. The tetracyclic compound, 5-amino-2 : 3-benzacridine, exists predominantly in the imino-form (V), however. Of the two N–H stretching vibration bands of 5-amino-2 : 3-benzacridine, the one at 3448 cm.$^{-1}$ falls into the intensity and frequency range typical of the amino N–H group, and the other at 3298 cm.$^{-1}$ into the range characteristic of the imine N–H group. The former band is similar to the single absorption of acridan, and it is due to the nuclear N–H group of (V), whilst the latter resembles that of 5-imino-10-methylacridan, being due to the exocyclic N–H group of (V) (Table 2, Figure).

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These findings are in accord with the expectations of molecular-orbital theory. The amino- or the imino-form of a given *N*-heteroaromatic amine may be obtained by the addition of a proton to the exocyclic or the nuclear nitrogen atom, respectively, of the corresponding anion (*e.g.*, VI). A σ N–H bond is formed in both cases, so that the π-electron energy change resulting from the protonation of a nitrogen atom of the anion determines which of the two tautomers is predominantly formed. According to first-order perturbation theory, the π-electron energy change, ΔE, resulting from the protonation of the anion (*e.g.*, VI) is given by

$$\Delta E = q_r \Delta\alpha_N \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where $\Delta\alpha_N$ is the increment in the Coulomb integral of a nitrogen atom when it is protonated, and q_r is the charge density of the corresponding carbanion q_x or q_n, depending upon the particular nitrogen atom protonated.

In the series of amines studied 5-amino-2 : 3-benzacridine is unique in that the corresponding carbanion has a charge distribution with $q_n > q_x$ (Table 2). Thus, by eqn. (1), the imine form (V) should be the stable tautomer, as found. In the carbanions corresponding to the remaining amines, apart from 5-aminoacridine, $q_x > q_n$, so that the amino-form should be the predominant tautomer in these amines. In the case of 5-aminoacridine, where $q_x = q_n$, recourse must be made to second-order perturbation theory, according to which the π-electron energy change resulting from the protonation of an amine anion (*e.g.*, VI) is given by

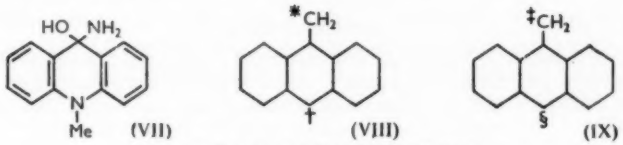
$$\Delta E = q_r \Delta\alpha_N + \pi_{r,r} \Delta\alpha_N^2/2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where $\pi_{r,r}$ is the self-polarizability of the atom r in the corresponding carbanion. The self-polarizabilities of the positions in the 9-anthrylmethyl anion occupied by nitrogen atoms in 5-aminoacridine, calculated by Coulson and Longuet-Higgins's method,[22] are 0·724 and 0·466 β^{-1} for the exocyclic and the nuclear position respectively, β being the carbon–carbon resonance integral. Thus the amino- and the imino-form of 5-aminoacridine should be equally stable in the first order, but the amino-tautomer should be the predominant form in the second order of approximation.

In aqueous solution, as in non-polar solvents, it is probable that the amino-form of 5-aminoacridine is the more stable tautomer. In water 5-aminoacridine has a pK_a value of [23] 9·99, and that of 5-imino-10-methylacridan is [24] 11·01, so that the amino-tautomer predominates over the imine by a factor of approximately 10. The pK_a value for 5-imino-10-methylacridan (II; R = Me) is reported [24] to be that for the equilibrium between the cation (III; R = Me) and the carbinol base (VII) in aqueous solution. However, the light-absorption characteristics in the visible region of the species in equilibrium are very similar,[24] and those species are, therefore, the cation (III; R = Me) and the imine (II; R = Me), which have similar spectra in the visible,[13,14] as the band of longest wavelength in the electronic spectrum of the carbinol base (VII) would be that of the diphenylamine chromophore in the ultraviolet region at [25] 290 mμ. Moreover, both of the species in equilibrium fluoresce in the visible region,[13,24] but diphenylamine has no visible fluorescence. The imine (II; R = Me) is hygroscopic, but water is combined only as solvent of crystallisation as the solid hydrate is yellow, and undergoes little colour change on dehydration, which is readily effected.[26] Similarly the ionisation constant reported [24] for 2-amino-10-methylacridinium bromide in water (pK_a = 11·85) probably governs the equilibrium between the cation and the corresponding imine. The pK_a value of 2-aminoacridine in water is [23] 8·04, so that the amino-tautomer predominates over the imine by a factor of approximately 6×10^3 in aqueous solution.

[22] Coulson and Longuet-Higgins, *Proc. Roy. Soc.*, 1947, **191**, *A*, 39.
[23] Albert, Goldacre, and Phillips, *J.*, 1948, 2240.
[24] Goldacre and Phillips, *J.*, 1949, 1724.
[25] Jaffe, *J. Chem. Phys.*, 1954, **22**, 1430.
[26] Albert and Ritchie, *J.*, 1943, 458.

The electronic spectra of 5-aminoacridine and its *N*-methyl derivatives are consistent with the conclusion that the amine tautomer predominates in aqueous and methanol solution, but not with the view that the imine form is more stable. The salient features of the visible spectra are [10,13,14,27,28] that 5-imino-10-methylacridan and the cation of 5-aminoacridine absorb at slightly shorter wavelengths ($\lambda_{max.}$ 400 mμ) than the neutral



Charges: * 0·286, † 0·286, ‡ 0·231, § 0·045.

molecule of 5-aminoacridine ($\lambda_{max.}$ 408 mμ) but with nearly the same intensity ($\varepsilon_{max.}$ ~10^4), whilst 5-dimethylaminoacridine absorbs at longer wavelengths ($\lambda_{max.}$ 420 mμ) with a lower intensity ($\varepsilon_{max.}$ $5{\cdot}6 \times 10^3$). In alternant systems the methyl group invariably gives rise to a bathochromic shift of the electronic spectrum, so that if 5-aminoacridine existed mainly in the imine form, 5-imino-10-methylacridan would absorb at longer wavelengths than the parent substance, which is not observed.

The visible absorption of 5-aminoacridine and its *N*-methyl derivatives is due to the promotion of an electron from the highest occupied to the lowest unoccupied molecular orbital of the π-electron system. The highest occupied π-orbital, which is filled with the lone-pair electrons of the exocyclic nitrogen atom, is derived from the non-bonding molecular orbital of the corresponding carbanion, which has the charge distribution (VIII). The lowest unoccupied π-orbital of the 9-anthrylmethyl anion has an energy of 0·683 β and the charge distribution (IX). On the substitution of nitrogen atoms into the carbanion the energy of the orbital is lowered by an amount depending upon the charge density at the position of substitution and the Coulomb integral increment of the nitrogen atom (*e.g.*, eqn. 1). In the amino-tautomer the exocyclic nitrogen atom is partly positively charged (*e.g.*, Ib) so that it has a larger Coulomb-integral increment than the nuclear nitrogen atom, whilst the reverse is true in the imino-tautomer (*e.g.*, IIb). The lowest unoccupied π-orbital in the amine tautomer is thus lower in energy than that of the imine form, as the charge density in (IX) is larger at the exocyclic than the nuclear position. The highest occupied π-orbital has the same energy in both tautomers, since there is the same charge density at the position of both nitrogen atoms in (VIII). Hence the amine tautomer should absorb at longer wavelengths than the imine form, as is found, in spite of the probable bathochromic effect of the methyl group in 5-imino-10-methylacridan.

The blue shift of the visible absorption of 5-aminoacridine on cation formation, a phenomenon which is quite unusual in the series of *N*-heteroaromatic amines,[4,5,10] can be similarly explained. When the nuclear nitrogen atom of 5-aminoacridine is protonated the energy of the highest occupied level is lowered more than that of the lowest unoccupied level, as the charge density at the nuclear position in (VIII) is larger than that in (IX) and the electronic transition energy is increased.

In 5-dimethylaminoacridine the steric hindrance between the methyl and *peri*-C–H groups has the effect that the nodal plane of the *p*-component in the lone-pair hybrid orbital of the amino-group nitrogen atom is twisted out of the plane of the acridine nucleus. The twist partially localises the lone-pair electrons upon the nitrogen atom of the amino-group, whilst the π-orbitals of the nucleus become less akin to those of the 9-anthrylmethyl anion and resemble more those of anthracene. The lowest unoccupied orbital of anthracene has a lower energy (0·414 β) than that of the 9-anthrylmethyl anion and a larger charge density (0·193 *e*) at the position corresponding to that of the nitrogen atom in acridine.

[27] King, Gilchrist, and Tarnoky, *Biochem. J.*, 1946, **40**, 706.
[28] Turnbull, *J.*, 1945, 444.

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The lowest unoccupied π-orbital in 5-aminoacridine has a higher energy than that of the dimethylamino-analogue, therefore, and the latter may be expected to absorb at longer wavelengths, and with a reduced intensity, since the partial localisation of the lone-pair electrons upon the dimethylamino-group results in a poor overlap between the electron distributions of the highest occupied and the lowest unoccupied orbitals.

Experimental

Materials.—1-Ethyl-1 : 2-dihydro-2- and 1-ethyl-1 : 4-dihydro-4-iminopyridine were prepared by Anderson and Seeger's method.[6] The remaining compounds were as in Albert, Goldacre, and Phillips [23] and in Albert and Ritchie,[26] and they were recrystallised to the m. p.s quoted.[23,26]

Infrared Spectra.—These were measured with a Perkin-Elmer model 12C spectrometer with a lithium fluoride prism and a quartz filter, and a Mervyn N.P.L. grating spectrometer using an *F*-centre filter for the 3μ region. The amines were examined in the range M/1000 to M/250, and the imines in the range M/250 to M/50, in carbon tetrachloride in a 5 cm. cell. 5-Aminoacridine was insufficiently soluble in carbon tetrachloride to allow the measurement of the intensity of the N–H stretching vibration absorptions with any precision, and it was examined in the region of M/100 in chloroform solution in a 1 cm. cell. The frequencies of the bands were reproducible to within 1 and 2 $cm.^{-1}$ with the prism and the grating instruments respectively, and the intensities to within about 5% with both spectrometers. The two instruments differed by up to 5 $cm.^{-1}$ in the measurement of frequency and up to 10% in the determination of intensities in the present work.

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Australian National University, Canberra.
The University, Exeter. [*Received, September 13th,* 1958.]

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252. *Dinitrogen Trioxide: Some Observations on the Electronic Spectrum and Structure.*

By (Mrs.) J. Mason (Banus).

The visible and near-ultraviolet absorption of dinitrogen trioxide, in toluene and other solvents at low temperatures, has been examined. The blue colour is due to a weak band in the red region, with $f \sim 4{\cdot}5 \times 10^{-4}$, $\lambda_{max.}$ 6620 Å in toluene, which is structureless, but otherwise resembles the nitrosoalkane band, and there is a strong band with $\varepsilon_{max.} > 2500$ below 3500 Å. The visible band shifts towards the blue with increasing polarity of the solvent.

Molecular-orbital, spectroscopic, and thermochemical considerations support the assignment of the trioxide visible band to a nitroso n_N–π^* transition, and the near-ultraviolet band to a π–π^* transition, in a nitro-nitroso-molecule with a π-only N–N bond. A nitrito-structure, or a nitro-nitroso-structure with a $(\sigma + \pi)$ N–N bond, would be more difficult to reconcile with the visible absorption and low heat of dissociation of dinitrogen trioxide.

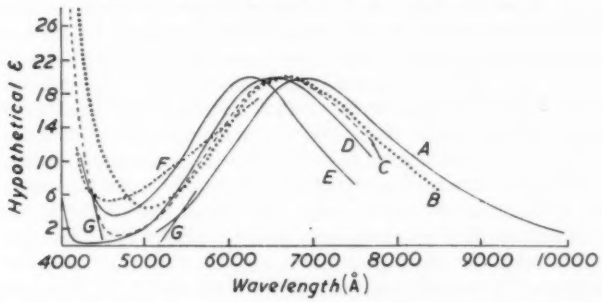
Although dinitrogen trioxide has been known [1] since 1816, and is readily recognised by its deep blue colour, precise knowledge of the molecule is lacking, probably because of its instability; it is 80% dissociated [2] into nitric oxide and nitrogen dioxide–dinitrogen tetroxide at 25° and 1 atm. Its rôle in the chamber process for sulphuric acid, and in

[1] Dulong, *Ann. Chim. Phys.*, 1816, **3**, 240.
[2] Beattie and Bell, *J.*, 1957, 1681.

nitrosation,[3] and its addition to olefins, are still being investigated, and opinions are divided as to the molecular constitution.

The visible and ultraviolet spectra have been examined, mostly at −80°, of standard trioxide solutions in toluene, ethyl ether, or mixed paraffins, made up by vacuum methods. Reproducible results were obtained with toluene as solvent, Beer's law being obeyed over the range studied, 0·007—0·038M. The spectrum is drawn in the Figure, and wavelengths and extinction coefficients are listed in the Table. The oscillator strength of the visible band is $f \sim 4{\cdot}5 \times 10^{-4}$, if the long tail beyond the limit of the Cary spectrophotometer at 7700 Å is estimated from the spectrum [4] of the carbon tetrachloride solution. All the

Spectrum of dinitrogen trioxide in various solvents.



Solvents: *A*, Carbon tetrachloride; *B*, acetic anhydride; *C*, toluene; *D*, diethyl ether; *E*, aqueous acid; *F*, liquid nitric oxide; *G*, toluene, plotted from Berl and Winnaker's results.[5]

solutions were opaque from about 3500 Å to 2000 Å. The extinction measurements are accurate to 5% or better at the higher densities, but less good at the minima, because of sensitivity there to the presence of impurities, and to misting of the cell windows.

There is no other quantitative measurement, in any solvent or without, for comparison, except Berl and Winnaker's [5] " transparency maximum " at 4750 Å for a toluene solution

Solvent	Dielect. const.	Temp.	$\varepsilon_{max.}$	$\lambda_{max.}$ (Å)	ε_{min}	$\lambda_{min.}$ (Å)	Ref.
Alkanes	2·0	−180°	—	~7200	—	—	—
Liq. NO ...	—	−150	0·56 (extrapolated)	~7000	0·14	4600	*a*
CCl_4	2·2	?	12	6960	<2	<5000	4
Toluene	2·4	−80	20·1	6620	1·1	4700	—
,, ...	,,	−50	—	—	<1	4750	5
Et_2O	4·3	−80	~20	6650	<1	4300	—
Ac_2O	20·5	20	—	6700	—	4770	*c*
Aq. acid.....	>80	20	—	6250	—	4800	*b*
,, ...	,,	,,	—	—	1	4780	5

[a] Vodar, *Compt. rend.*, 1937, **204**, 1467. [b] Bunton and Stedman, *J.*, 1958, 2440. [c] Deschamps, personal communication.

of the trioxide at −50°; their results can be plotted as the two straight lines (*G*) in the Figure. They studied only the 4400—5600 Å region, and found Beer's law to be obeyed for 0·32—0·67M concentrations of trioxide.

Quantitative spectra were not obtained with the other solvents (see Experimental section). Dissociation and loss of nitric oxide, which could only be detected in toluene solutions at −45° and above, occurred well below −80° with the aliphatic hydrocarbons,

[3] Hughes, Ingold, and Ridd, *J.*, 1958, 58.
[4] Seel and Sauer, *Z. anorg. Chem.*, 1957, **292**, 1.
[5] Berl and Winnaker, *ibid.*, 1933, **212**, 113.

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in which the trioxide is less soluble, and there was some hydrolysis in the ether solutions. Qualitative curves, for unknown concentrations of trioxide in various solvents, are plotted in the Figure so as to have an arbitrary $\varepsilon_{max.}$ of 20, although $\varepsilon_{max.}$ commonly varies with the solvent. These solutions also are described in the Table.

The low-temperature spectra show that nitrogen dioxide is absent, for this would absorb [6] moderately strongly ($\varepsilon \sim 100$) at the minimum of the trioxide's absorption, and its banded spectrum is readily recognised. Dinitrogen tetroxide, however, might be present, for its absorption,[6,7a] which begins at about 3900 Å and reaches $\varepsilon_{max.}$ 170 (for the vapour) at 3400 Å, would be masked by the intense ultraviolet absorption of the trioxide that begins at about 4500 Å and reaches $\varepsilon_{max.} > 2500$ below 3500 Å.

Dissociation of the trioxide should be small, however; at −80° and 0·6 atm. (0·038M expressed as a gas pressure), gaseous dinitrogen trioxide is 2% dissociated, according to a rather extended extrapolation of the equilibrium equations [2] for 5°—45°; and it is likely that toluene or ether stabilises the trioxide, as the tetroxide is stabilised relative to nitrogen dioxide by aromatic molecules and Lewis bases.[7] The tetroxide forms complexes [7] with these, but according to the spectra the trioxide does not, under the conditions described; neither does it cleave the ether, although this has been reported [8] as taking place readily. Study of some related solutions (see Experimental) showed that stronger reagents than dinitrogen trioxide, and higher temperatures than −80°, are needed for ether cleavage. If the trioxide were ionised, the absorption of the nitrosyl ion [9] and of the nitrite ion [10] would be hidden by the trioxide's ultraviolet band, but such species would not be stable in these organic solvents.

The spectra appear to be temperature-invariant, except for evidence of dissociation at higher temperatures. In none of the solutions could any trace of vibrational structure be detected in the visible band, and this is in contrast to the visible band of trifluoronitrosomethane,[11] which is very similar in shape, location, and intensity but shows considerable (though not very sharp) structure. This difference may be related to the dissociation energies of the bonds to the nitroso-group, about 50 kcal./mole for the *C*-nitroso-compound [11] as against 10·3 for the trioxide: [2] the energy at the long-wavelength limit of the trioxide band, about 10,000 Å, is over 20 kcal./mole, so that dissociation may well follow absorption. The nitrosoalkane band does not have the trioxide band's long tail in the red region, so that the oscillator strength is slightly larger for the trioxide, and the band origin perhaps 0·3 ev lower, since the trioxide molecule is probably vibrationless at −80° in the electronic ground state.

Nature of the Transitions.—If dinitrogen trioxide is a nitronitroso-compound (see below), we should expect to find in the electronic spectrum a low-energy low-intensity band due to a nitroso n_N–π^* transition (where n refers to non-bonding electrons, and π^* to the lowest unfilled π orbital) absorbing near 7000 Å in the nitrosoalkanes.[11,12] Sidman [13] has assigned the nitroso visible band to an n_O–π^* transition, on intensity grounds, but the (small) variations of the n–π^* intensities are not yet understood, and the assignment to the n_N electrons is preferred here on energetic grounds [cf. the n_N–π^* bands of azomethane [14] near 3000 Å ($\varepsilon_{max.} \sim 5$), and diazomethane [15] near 4000 Å ($\varepsilon_{max.} \sim 3$)]. The n_O–π^* bands are considered to be at shorter wavelengths because of the greater electronegativity of oxygen (though this energy increment may be offset to some extent by a higher p character in the

[6] Hall and Blacet, *J. Chem. Phys.*, 1952, **20**, 1745.
[7] Addison and Sheldon, *J.*, (*a*) 1958, 3142; (*b*) 1956, 1941, 2705, 2709; Ling and Sisler, *J. Amer. Chem. Soc.*, 1953, **75**, 5191 and earlier papers.
[8] (*a*) Wieland, *Ber.*, 1921, **54**, 1782; (*b*) Reihlen and Hake, *Annalen*, 1927, **452**, 48.
[9] Deschamps, *Compt. rend.*, 1957, **245**, 1432.
[10] Sidman, *J. Amer. Chem. Soc.*, 1957, **79**, 2669.
[11] Mason (Banus), *J.*, 1957, 3904.
[12] Orgel, *J.*, 1953, 1276.
[13] Sidman, *Chem. Rev.*, 1958, 689.
[14] Ramsperger, *J. Amer. Chem. Soc.*, 1928, **50**, 123.
[15] Brinton and Volman, *J. Chem. Phys.*, 1951, **19**, 1395.

n_O than in the n_N electron): *e.g.*, 2700 and 2800 Å ($\varepsilon_{max.}$ ~2 and 10) for the alkyl nitroso- and nitro-compounds respectively [11] and 2800 Å ($\varepsilon_{max.}$ ~10) for aliphatic ketones. There is as yet no certain basis for these assignments.

The trioxide spectrum has not been examined in the near-infrared region, and n–π^* transitions in the near ultraviolet region will be hidden by the intense absorption there, since they are largely overlap-forbidden; the strong ultraviolet band is probably due to a fairly low-energy π–π transition (these are all allowed).

Solvent Shifts.—Blue shifts with increase in polarity of the solvent are characteristic, and occasionally diagnostic, of n–π^* bands,[16] because interaction of the n electrons with polar, perhaps hydrogen-bonding, solvent molecules stabilises the ground state relative to the excited state in the transition. Such blue shifts are found for alkyl *C*-, *N*-, and *O*-nitroso n_N–π^* bands,[11] and may be larger for dinitrogen trioxide than for *C*-nitroso-compounds, since the trioxide molecule is more polar than a nitrosoalkane, and the shifts are very large for the dialkyl *N*-nitrosamine bands. π–π Bands in systems of this sort are usually much less affected by changes in the polarity of the solvent.

From wavelengths listed in the Table, we can estimate a blue shift of 200 cm.$^{-1}$ for ether solutions of the trioxide compared with toluene solution, and 1000 cm.$^{-1}$ for aqueous acid solution compared with toluene; these shifts are increased if an aliphatic hydrocarbon is taken as reference solvent. For trifluoronitrosomethane the blue shift is 100 cm.$^{-1}$ for ether solution, or 350 cm.$^{-1}$ for aqueous solution, each relative to aliphatic hydrocarbon solvent; the corresponding figures for *N*-nitrosamines are 150 and 2500 cm.$^{-1}$, while the blue shifts for alkyl nitrites are small. On the other hand, the blue shifts for the n_O–π^* band of nitromethane [17] are 700 cm.$^{-1}$ for dioxan and 900 cm.$^{-1}$ for aqueous, relative to aliphatic hydrocarbon, solution, and there is a red shift of 600 cm.$^{-1}$ for toluene solution.

The dinitrogen trioxide solvent shifts thus support the assignment of the visible band to an n–π^* transition, and if it is from nitrogen rather than from oxygen, the trioxide is behaving more like an *N*-nitroso- than a *C*- or *O*-nitroso-compound. The sequence of bands for the different solvents follows the order of the dielectric constants, with the exception of the acetic anhydride solution spectrum; however this was observed without special precautions, such as rigorous drying of the solvent, which were found to be necessary before consistent spectra of dinitrogen tetroxide could be obtained in it, and the 3400 Å tetroxide band shifts to the red in acetic acid, as compared with anhydride, solution.[7a]

Structure of Dinitrogen Trioxide.—Direct evidence as to the molecular constitution of the trioxide is lacking. The *X*-ray study [18] of the solid (m. p. *ca.* −103°) at −115° was inconclusive; it is reported [19] to exchange with nitric oxide at −118°. The liquid (b. p. *ca.* 3·5°) is diamagnetic and non-conducting,[8a] and less likely to be ionised than the tetroxide.[20] Tarte,[21] who examined the infrared spectrum in the sodium chloride region of gaseous dinitrogen trioxide (at room temperature in the presence of its dissociation products and a little nitrous acid), found that it could not be assigned in terms of a nitrito-structure O:N·O·N:O, and that fundamental frequencies for a nitronitroso-molecule $O_2N{\cdot}N{:}O$ could be chosen to fit corresponding ones in nitric oxide, nitrogen dioxide, and dinitrogen tetroxide.

Supporters of a nitronitroso-structure for dinitrogen trioxide include Wieland,[8a] Ingold and Ingold,[22] Walsh [22] (with the dubious argument that the bond is probably N–N since the odd electron in nitric oxide and in nitrogen dioxide is nearer to the nitrogen atom than to oxygen), Addison and Lewis,[22] and Coulson and Duchesne.[23]

[16] Kasha, *Discuss. Faraday Soc.*, 1950, **9**, 14; McConnell, *J. Chem. Phys.*, 1952, **20**, 700.
[17] Bayliss and Brackenridge, *J. Amer. Chem. Soc.*, 1955, **77**, 3959.
[18] Reed and Lipscomb, *Acta Cryst.*, 1953, **6**, 781.
[19] Leifer, *J. Chem. Phys.*, 1940, **8**, 301.
[20] Addison, Lewis, and Thompson, *J.*, 1951, 2838.
[21] Tarte, *Bull. Soc. roy. Sci. Liège*, 1953, 276.
[22] Ingold and Ingold, *Nature*, 1947, **159**, 743; Walsh, *J.*, 1953, 2272; Addison and Lewis, *Quart. Rev.*, 1955, **9**, 115.
[23] Coulson and Duchesne, *Bull. acad. roy. Belg.*, 1957, **43**, 522.

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A nitrito-structure is preferred by Sidgwick;[24] he and Cartmell and Fowles[25] quote Leifer's opinion[19] that the rapid exchange of ^{14}N in nitric oxide and ^{15}N in nitrogen dioxide at −35° proves the two nitrogen atoms in the trioxide to be equivalent. However there can be other routes to the exchange than the dinitrogen trioxide molecule. Packer and Vaughan[26] consider that the trioxide behaves (in acid nitrite solution) as an equilibrium mixture of the nitrito- and the nitronitroso-form, but such an equilibrium is unlikely in the solutions studied here, since the visible absorption is temperature-invariant and obeys Beer's law within the experimental limits (exact measurement of optical densities above or below −80° was difficult); and the spectrum might be expected to show the nitrite structure below 4000 Å, as do trioxide solutions when partial hydrolysis has occurred.

Nature of the N–N *Bond.*—The presence in the trioxide of a weak bond comparable to the N–N bond in the tetroxide is suggested by the heats of dissociation, respectively[2,27] 10·3 and 12·875 kcal./mole (and it is likely that in the trioxide[21] as in the tetroxide[23] the geometries and bond properties are similar to those of the molecular dissociation products). The N–N single-bond energy term, however, is much higher than this, if somewhat less than the N–N bond dissociation energy for hydrazine,[28] 60 kcal./mole. That the N–N bond type is different in the tetroxide and in the hydride is borne out by the stretching frequencies, respectively[29] 265 and 850 $cm.^{-1}$, and by the lengths, 1·75 Å for the gaseous tetroxide[30] against 1·47 Å for hydrazine.[31] The values are not known for the trioxide, but from the energy of dissociation the analogy between the trioxide and tetroxide, in contrast to the hydride, seems plausible. The nitric oxide dimer, which has a dissociation energy[32a] of 4 kcal./mole and is diamagnetic as a solid[32b] and as a liquid,[32c] is sometimes included in this comparison;[21,23] however the molecule in the crystal[32d] is not ON·NO, but a rectangle of two nitric oxide molecules head-to-tail.

From molecular-orbital calculations on the tetroxide molecule, Chalvet and Daudel[33] derive a total N–N bond order ($\sigma + \pi$) of 1·164, but this is difficult to reconcile with the length and weakness of the bond. A more convincing description[23,30] is that the tetroxide N–N bond is formed by π overlap only, with no (resultant) σ component, for the molecule is planar even in the gas phase, with an N–N bond 0·27 Å longer than the normal single bond. Coulson and Duchesne[23] derive a total bond order of about $\frac{1}{3}$ for this π-only N–N bond; this figure is obtained by use of the normal double-bond value for the resonance integral, and a better approximation is to take the latter as proportional[34] to the overlap (estimated[35] for Slater orbitals, for N–N bond lengths of 1·24 and 1·75 Å); the bond order then reduces to about 0·1. A plot of N–N bond orders against lengths extrapolates readily to a bond order of 0·1 (or $\frac{1}{4}$) for the long N–N bond. The curvature between bond orders 1 and 3 is greater than for C–C bonds, perhaps because the n_N electrons repel more strongly at closer approach.

The nitrogen lone pairs that overlap in the centre of the molecule can be considered to interact to form fully occupied σ and σ^* orbitals, somewhat antibonding in total effect.

Although fewer measurements are available for the trioxide than for the tetroxide

[24] Sidgwick, " The Chemical Elements and their Compounds," Oxford Univ. Press, 1950, **1**, 688.
[25] Cartmell and Fowles, " Valency and Molecular Structure," Butterworths, London, 1956, 162.
[26] Packer and Vaughan, " Organic Chemistry," Oxford Univ. Press, 1958, 148.
[27] Giauque and Kemp, *J. Chem. Phys.*, 1938, **6**, 40.
[28] Cottrell, " The Strengths of Chemical Bonds," Butterworths, London, 1954.
[29] Wiener and Nixon, *J. Chem. Phys.*, 1957, **26**, 906; Fresenius and Karweil, *Z. phys. Chem.*, 1939, *B*, **44**, 1.
[30] Smith and Hedberg, *J. Chem. Phys.*, 1956, **25**, 1282.
[31] Anderson and Kistiakowsky, *ibid.*, 1943, **11**, 6.
[32] (*a*) Rice, *ibid.*, 1936, **4**, 367; Eucken and d'Or, *Nachr. Ges. Wiss. Göttingen, Math.-physik. Kl.*, 1932, 107; (*b*) Lips, *Helv. Chim. Acta*, 1935, **8**, 247; (*c*) Bizette, and Tsai, *Compt. rend.*, 1938, **206**, 1288; (*d*) Dulmage, Meyers, and Lipscomb, *J. Chem. Phys.*, 1951, **19**, 1432.
[33] Chalvet and Daudel, *J. Chim. phys.*, 1952, **49**, 77.
[34] Mulliken, *ibid.*, 1949, **46**, 712.
[35] Mulliken, Rieke, Orloff, and Orloff, *J. Chem. Phys.*, 1949, **17**, 1248.

molecule, two criteria for a π-only N–N bond, a low dissociation energy and similar bond properties in the compound molecule and in its molecular dissociation products,[21] appear to be fulfilled.

A consequence of a π-only N–N bond is that the n–π^* (and π–π^*) transitions should require less energy than if the trioxide molecule had a ($\sigma + \pi$) N–N bond, or a nitrito-structure; the numbers of π electrons in the three forms are respectively 4, 6, and 6, so that in the π-only N–N bonded molecule transitions can be made to the non-bonding molecular orbital, which is some way below the lowest anti-bonding orbital. Thus for the π-only form it is likely, and for the other structures less likely, that the extension of the delocalisation to cover five nuclei, instead of two in the nitrosoalkane, brings down the π^* orbital, to compensate for the shrinkage of the nitroso n_N orbital by the nitro-group. This would explain the similar energies of the nitrosoalkane and trioxide visible bands, for the n_N–π^* absorption of alkyl *N*-nitroso(and *O*-nitroso)-compounds is in the near ultra-violet region.

The charge in the non-bonding molecular orbital of the nitronitroso-molecule is very largely on the nitro-oxygen atoms, and in the higher bonding orbital much of the charge is on the nitroso-oxygen. Because of the reduced overlap, the lowest-energy π–π transition may absorb less strongly than the others. This charge distribution in the non-bonding molecular orbital might also be expected to reduce the n_N–π^* transition probability compared with that of a nitrosoalkane (the antibonding orbital is more evenly distributed over the nuclei), but the oscillator strengths are similar; a higher *s* component in the trioxide nitroso n_N electrons would be a compensating factor.

A nitrito-structure has a higher delocalisation energy than a nitronitroso-structure (as is usual for a branched system compared with its straight-chain isomer), and this, together with the extra σ bond, might be expected to give the nitrito-form the advantage in stability over the π-only N–N-bonded form. The balance could be restored, however, if, as seems likely, the energy term is much lower for a "single" than for a "double" N–O bond, as is the case for N–N and O–O bonds.[28,36]

Justification for the π-only bond in the trioxide (and in the tetroxide) can be found in the higher *s*–*p* promotion energy [37] of nitrogen (11 ev) and oxygen (nearly 16 ev) than of carbon (4 ev), which has a lower nuclear charge and in which the *s* electron goes into an empty *p* orbital. The large promotion energy outweighs the fairly low further energies to form valence states [38] (3·3 for nitrogen, 2 for oxygen, against 4 ev for carbon). This favours the π-only N–N bonded structure, which has more n electrons (12 n_O, 6 n_N) than either the ($\sigma + \pi$) N–N-bonded form (12 n_O, 2 n_N), or the nitrito-form (10 n_O, 4 n_N), since n electrons usually are largely *s* in character, unless they can delocalise; the economy in promotion energy more than offsets any weakening of the bonds due to higher-valence shell repulsions.

A really high *s* component in the n_N orbitals that overlap in the π-only N–N bond would reduce the repulsion, for at 1·75 Å the 2sσ–2sσ overlap [35] ($S_\sigma = 0{\cdot}15$) for nitrogen is less than half the sp, sp^2, or sp^3 overlap ($S_\sigma = 0{\cdot}37$). However the repulsion of the n_O electrons in the nitro-group sets a lower limit to the ONO angle, 133° in the tetroxide (134° in the dioxide), so that the tetroxide's nitrogen atoms are roughly sp^2 hybridised, with a rather higher *p* component in the N–N σ bond-plus-antibond than in the bonds to oxygen. The bonding π overlap [35] is low ($S_\pi = 0{\cdot}07$), but can outweigh a larger repulsive S_σ overlap: according to Mulliken's magic formula [39] the energy terms are respectively proportional to $S_\pi/(1 + S_\pi)$ and to $S_\sigma^2/2$.

The overlap between adjacent n_N and n_O orbitals in the nitroso-group is not negligible (it is [35] 0·1 for sp^2, or 0·4 for pure *s* orbitals, for a bond distance of 1·2 Å) and will split

[36] Gray, *Trans. Faraday Soc.*, 1955, **51**, 1367; Samuel, *Rev. Mod. Phys.*, 1946, **18**, 103.
[37] Atomic Energy Levels, Nat. Bur. Stand., Washington, circular no. 467, 1949, **1**, 22, 32, 46.
[38] Skinner and Pritchard, *Trans. Faraday Soc.*, 1953, **49**, 1254.
[39] Mulliken, *J. Phys. Chem.*, 1952, **56**, 295.

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the n_N and n_O energy levels further apart, lowering the " n_N–π^* " and raising the " n_O–π^* " transition energies. This factor should be taken into account in a comparison of nitroso n–π^* energies with those of carbonyl or (*trans*-)azo-groups, for example, where this n-orbital overlap is absent.

Attempts to find the maximum of the intense trioxide absorption in the near ultraviolet region were unsuccessful, possibly because of dissociation of the trioxide in solutions that were weak enough for the absorption to be measurable. This problem could perhaps be attacked by a low-temperature study of a trioxide film, or of a solution with a very small absorbing path, which should also be examined in the near infrared region.

Experimental

The spectra were measured with a Cary recording spectrophotometer. A doubly-jacketed metal cell [40] (with some modifications) was used at −183°, −80°, and at −45° (melting chlorobenzene), the outer jacket being filled with dry nitrogen (since it was not vacuum-tight at low temperatures) and hot air blown on the outer windows.

The ether and toluene solvents were dried over sodium wire and distilled through a very efficient column; middle fractions were taken, and kept over bright sodium wire. The mixed hydrocarbon solvent, 6 : 1 *iso*pentane–methyl*cyclo*hexane, was purified for ultraviolet transmission by prolonged shaking with sulphuric acid, then with potassium hydroxide pellets to remove sulphur dioxide. Nitric oxide was prepared by reduction of nitrite by ferrous ion, the method [41] having been adapted for use with a vacuum system.

Solutions of dinitrogen trioxide and nitrogen dioxide were made up by vacuum methods to exclude moisture or air, and where vacuum grease was unavoidable, Silicone grease was used. The dioxide or trioxide was made from measured amounts of nitric oxide and dry oxygen, and distilled *in vacuo* into the frozen solvent in a Carius tube, which was sealed and kept frozen until required. The Carius tubes and metal cell were dried and flushed out with dry nitrogen before use, and a dry-nitrogen train was attached to the cell in use. The spectra were measured as quickly as possible because of misting of the cell windows.

Dinitrogen Trioxide in Toluene.—Twelve solutions, 0·007—0·038M in trioxide, were examined, and the absorption found to obey Beer's law. There was no trace of nitrous acid structure in any of the toluene spectra, although these were examined with the same technique as for the ether spectra.

Dinitrogen Trioxide in Ether.—While the spectra were being recorded, the visible and ultraviolet bands of the trioxide became fainter as the banded spectrum of nitrous acid [42] emerged. By comparison with a standard solution of nitrous acid in ether it was found that the formation of acid by a trioxide solution left in the low-temperature cell until colourless was almost quantitative, according to the equation $N_2O_3 + H_2O \rightleftharpoons 2HO{\cdot}NO$, so that no dissociation had occurred. Hydrolysis of the trioxide, and the reverse reaction, are known to be slow. If the visible band of the ether trioxide solution is assumed to have $\varepsilon_{max.}$ ~20, the nitrous acid coexisting with trioxide is equivalent to the trioxide missing. This points to the absence of any ether–trioxide complex, nitrito-trioxide molecules, or products of ether cleavage.

The only other solvent besides ether to give some (slight) nitrous acid structure in the spectrum was the hydrocarbon mixture, despite the purification procedure. In acetic anhydride the solvent could act as scavenger. Quantitative spectra of the trioxide, as of the tetroxide,[7a] should be obtainable with ether.

Dinitrogen Trioxide in Aliphatic Hydrocarbons.—The trioxide's visible band could only be roughly estimated, because of low solubility at temperatures just above −183°, and misting of the cell windows. In the most dilute solutions studied, about 0·001M, the ultraviolet absorption was too strong to be measured, so that $\varepsilon_{max.}$ was probably above 2500.

Other Solutes.—Solutions of nitrogen dioxide and of nitrosyl perchlorate in dry ether or dioxan at −80° and at room temperature were examined. The nitrosyl perchlorate solution at room temperature developed a little ethyl nitrite with time, as if the ether was slowly cleaved

[40] Passerini and Ross, *J. Sci. Instr.*, 1953, **30**, 274.
[41] *Inorg. Synth.*, 1946, **2**, 126.
[42] Tarte, *Bull. Soc. chim. belges*, 1950, **59**, 365; Deschamps, personal communication; Ungnade and Smiley, *J. Org. Chem.*, 1956, **21**, 993.

(the spectrum was compared with that of ethyl nitrite in ether). There was some hydrolysis. An ethyl nitrite spectrum was also obtained from a solution of nitronium hydrogen pyrosulphate in dry ether or dioxan at room temperature. It seems, then, that stronger reagents than dinitrogen trioxide, and temperatures above −80°, are required to cleave ethyl ether.

The intense near-ultraviolet absorption was shown by all the trioxide solutions, and by no others. In many of the other solutions studied, the alkyl nitrite or nitrous acid spectra overlaid an absorption rising gently from 4000 to 3000 Å, due perhaps to dinitrogen tetroxide.

The author thanks Dr. C. A. Bunton for drawing her attention to the spectroscopy of dinitrogen trioxide solutions at low temperatures, and Dr. R. J. Gillespie for samples of the nitrosyl and nitronium salts.

WILLIAM RAMSAY AND RALPH FORSTER LABORATORIES,
UNIVERSITY COLLEGE, LONDON, W.C.1. [*Received, October 22nd*, 1958.]

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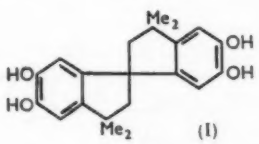
253. *Some Bis*-1 : 1′-spiro*Indanes*.

By WILSON BAKER and H. L. WILLIAMS.

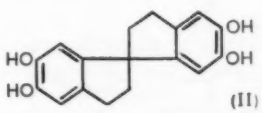
Bis-3 : 4-dimethoxyphenethyl ketone (III) reacts with phosphorus oxychloride in benzene to give 5 : 6 : 5′ : 6′-tetramethoxybis-1 : 1′-*spiro*indane (V), *via* the indene (IV). The structure of the spiran (V) was established by oxidation to the known *spiro*-anhydride (VI) of the acid (VII), and to the diketone (VIII) which possesses two reactive methylene groups.

The oxidation of the derived tetrahydroxybis-1 : 1′-*spiro*indane (II) throws light on the known remarkable behaviour on oxidation of the related *C*-tetramethyl derivative (I).

CERTAIN phenols, in which electrophilic substitution occurs *para* to a hydroxyl group, condense with acetone under acidic conditions to give derivatives of 3 : 3 : 3′ : 3′-tetramethylbis-1 : 1′-*spiro*indane, a reaction which probably involves the intermediate formation of phorone. Thus catechol and acetone give 5 : 6 : 5′ : 6′-tetrahydroxy-3 : 3 : 3′ : 3′-tetramethylbis-1 : 1′-*spiro*indane (I),[1,2] *o*-cresol and acetone give 6 : 6′-dihydroxy-3 : 3 : 5 : 3′ : 3′ : 5′-hexamethylbis-1 : 1′-*spiro*indane,[3,4] and pyrogallol and acetone give 5 : 6 : 7 : 5′ : 6′ : 7′-hexahydroxy-3 : 3 : 3′ : 3′-tetramethylbis-1 : 1′-*spiro*indane.[5]



(I)



(II)

The biss*pirocyclo*pentene system in (I) is remarkably stable. It survives vigorous treatment with nitric acid and ethanol which causes oxidation to the related bis-*o*-quinone in 80% yield;[6,1] this is a most unusual way to prepare an *o*-quinone. Again aerial oxidation of the spiran (I) in alkaline solution causes symmetrical rupture of both catechol nuclei without degradation, to give in 75% yield 2 : 3 : 2′ : 3′-tetra(carboxymethylene)-4 : 4 : 4′ : 4′-tetramethylbis-1 : 1′-*spirocyclo*pentane.[2] Neither of these properties is shown by 5 : 6-dihydroxyindane; this yields an unstable red *o*-quinone only by oxidation with silver oxide in ether.[2] It is probable, therefore, that the abnormal properties of the spiran (I) are connected with the fact that both the carbon atoms attached to each catechol

[1] Baker, *J.*, 1934, 1678.
[2] Baker and McGowan, *J.*, 1938, 347.
[3] Fisher, Furlong, and Grant, *J. Amer. Chem. Soc.*, 1936, **58**, 820.
[4] Baker and Besly, *J.*, 1939, 1421.
[5] Baker and Besly, *J.*, 1939, 195.
[6] Fabinyi and Széky, *Ber.*, 1905, **38**, 2307.

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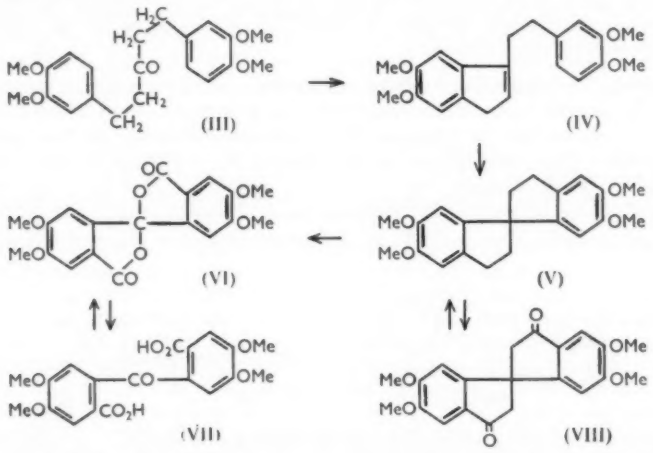
nucleus are quaternary, thus not only preventing attack at these positions and at the carbon atoms themselves, but also oxidation *via* intermediate methylenequinones.

To obtain further information, the synthesis of 5 : 6 : 5′ : 6′-tetrahydroxybis-1 : 1′-*spiro*indane (II) was undertaken and its properties were investigated. In brief the unsubstituted methylene groups at positions 3 and 3′ do not permit the abnormally easy oxidation to the bis-*o*-quinone, and no clear-cut reaction but much degradation occurs as the result of alkaline oxidation.

The synthesis was achieved as follows. Di-3 : 4-dimethoxyphenethyl ketone (III), prepared by catalytic reduction of diveratrylideneacetone, undergoes cyclodehydration to 5 : 6 : 5′ : 6′-tetramethoxybis-1 : 1′-*spiro*indane (V) in 91% yield when boiled with phosphorus oxychloride in benzene. Cyclodehydration of the ketone (III) with polyphosphoric acid for 2½ hours also gave the spiran (V) and a little of the isomeric 3-(3 : 4-dimethoxyphenethyl)-5 : 6-dimethoxyindene (IV); but after reaction for only 1 hour the yield of the spiran was very small and that of the indene much higher. The indene, therefore, is an intermediate in the production of the spiran (V), and was converted into it by phosphorus oxychloride in boiling benzene or by stannic chloride in chloroform.

Cyclodehydration of the ketone (III) to a saturated compound, $C_{17}H_{12}(OMe)_4$, might theoretically proceed in twenty-three different ways to give structurally isomeric tetramethoxy-derivatives of seven parent hydrocarbons, and there are in addition twenty racemic geometrical isomerides. A unique solution to the problem is afforded by the following facts which establish the structure as racemic 5 : 6 : 5′ : 6′-tetramethoxybis-1 : 1′-*spiro*indane (V).

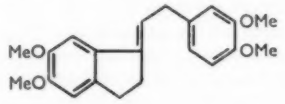


(*a*) When oxidised with potassium permanganate the product gave the known *spiro*-anhydride [7] (VI) of 4 : 5 : 4′ : 5′-tetramethoxybenzophenone-2 : 2′-dicarboxylic acid (VII). This proves that there is *one* single-carbon bridge between the two dimethoxyphenyl nuclei and establishes the two new positions of attachment of carbon atoms to these nuclei. The free dicarboxylic acid (VII), not previously known, was obtained by alcoholic alkaline hydrolysis of the *spiro*-anhydride followed by acidification. (*b*) Oxidation of the product (V) by chromium trioxide gave a diketone (VIII), which on Clemmensen reduction reverted to the starting material (V). The ultraviolet absorption of the diketone shows that the carbonyl groups are each adjacent to an aryl nucleus, so that in the cyclodehydration product there must be methylene groups similarly attached. (*c*) The diketone (VIII) gives a dibenzylidene derivative when condensed with benzaldehyde in presence of ethanolic sodium

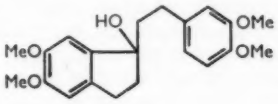
[7] Oliverio and Boumis, *Gazzetta*, 1951, **81**, 581.

ethoxide. This establishes the presence of a methylene group adjacent to each carbonyl group in the diketone, and therefore of a $-CH_2 \cdot CH_2-$ group attached to each dimethoxyphenyl nucleus in (V), thus leading to (V) as the only structure for the saturated, cyclised product $C_{17}H_{12}(OMe)_4$.

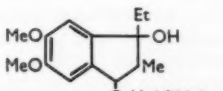
The intermediate, unsaturated compound is almost certainly the indene (IV) rather than the isomeric methyleneindane (IX), and it must result from the dehydration of the



(IX)



(X)



(XI)

initially formed tertiary alcohol (X). There are several reasons for preferring the indene structure (IV), and an extremely close analogy for its formation is provided by dehydration of the tertiary indanol (XI) to the indene and not the (known) ethylideneindane.[8]

The ultraviolet absorption spectra of a few of the substances mentioned in this paper are recorded in the Table.

The spectra of 5 : 6 : 5′ : 6′-tetramethoxybis-1 : 1′-*spiro*indane (V) and of its 3 : 3 : 3′ : 3′-tetramethyl derivative [tetramethyl ether of (I)] [1] are almost identical. The spectrum of the diketone (VIII) is very similar to that of 2 : 2′-diacetyl-4 : 5 : 4′ : 5′-tetramethoxydibenzyl [9] which contains the same chromophoric groups; if the carbonyl groups in the oxidation product of (V) were in positions 2 and 2′ the spectrum would resemble that of the parent bis-1 : 1′-*spiro*indane (V) and this is not the case.

Ultraviolet absorption maxima in ethanol.

Substance	λ (mμ)	$\log_{10}\varepsilon$	λ (mμ)	$\log_{10}\varepsilon$	Substance	λ (mμ)	$\log_{10}\varepsilon$	λ (mμ)	$\log_{10}\varepsilon$
(V)	232	4·16	287, 291	3·99, 3·98	(VIII)	236	4·51	268·5, 311·5	4·26, 4·16
Me_4 ether of (I)	232	4·22	286, 291	4·01, 3·99	(IV)	218	4·45	273, 296	4·00, 3·73

Experimental

Di-3 : 4-*dimethoxyphenethyl Ketone* (III).—Diveratrylideneacetone, prepared from veratraldehyde and acetone,[10] was obtained in different experiments either as bright yellow needles, m. p. 84°, or plates, m. p. 122—123°. Previous workers [11,12] have recorded m. p. 84°, except Haworth and Lamberton [13] who obtained both forms which they probably rightly regarded as dimorphic modifications; it is, however, just possible that the two might be geometrical isomerides. Catalytic reduction of the diveratrylideneacetone (64 g.) in ethyl acetate (400 ml.) in presence of Raney nickel at 4 atm. and room temperature until a colourless solution was obtained, filtration, and concentration gave the ketone (III) as colourless needles (62 g.; 95%), m. p. 85° (oxime, m. p. 138·5°; lit.,[10] m. p. 138—139°; semicarbazone, m. p. 189°).

Cyclodehydration of Di-3 : 4-*dimethoxyphenethyl Ketone* (III).—(a) *With phosphorus oxychloride.* 5 : 6 : 5′ : 6′-*Tetramethoxybis*-1 : 1′-spiro*indane* (V). The ketone (11·4 g.) was boiled for 4 hr. with phosphorus oxychloride (45 ml.) in anhydrous benzene (114 ml.), and the solution which had become deep blue was then cooled and added to ice-water (400 g.). The combined benzene layer and an extract were shaken 3 times with 5% aqueous sodium hydroxide, then with water, dried, and distilled, and the residue which solidified was crystallised from methanol (30 ml.) at 0°, giving 5 : 6 : 5′ : 6′-*tetramethoxybis*-1 : 1′-spiro*indane* (V) as radiating crystal aggregates (9·64 g.), m. p. 80—81° [Found: C, 73·9; H, 6·9; OMe, 35·4. $C_{17}H_{12}(OMe)_4$ requires C, 74·1; H, 7·1; OMe, 36·5%]. No hydrogen was absorbed by this compound on attempted catalytic reduction.

[8] Müller, Mészáros, Körmendy, and Kucsman, *J. Org. Chem.*, 1952, **17**, 787.
[9] Battersby and Binks, *J.*, 1955, 2897.
[10] Sugasawa and Yoshikawa, *J.*, 1933, 1584.
[11] Stobbe and Haertel, *Annalen*, 1909, **370**, 104.
[12] Dickinson, Heilbron, and Irving, *J.*, 1927, 1892.
[13] Haworth and Lamberton, *J.*, 1946, 1003.

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(b) ***With polyphosphoric acid.*** **3-(3 : 4-*Dimethoxyphenethyl*)-5 : 6-*dimethoxyindene*** **(IV).** **(i)** The finely powdered ketone (III) (8 g.) was added to polyphosphoric acid (84% of P_4O_{10}; 80 g.) at 60°, and the mixture stirred at this temperature for 1 hr. The dark product was then stirred into 5% hydrochloric acid (150 ml.) at 0°, and after being kept at room temperature for some hours, the product was collected, washed several times with 5% aqueous sodium hydroxide and then with water, dried *in vacuo*, and extracted with ether (3 × 50 ml.). The ether-insoluble material crystallised from methanol as needles (1·8 g., 24%), m. p. 135° [Found: C, 74·2; H, 7·0; OMe, 36·6. $C_{17}H_{12}(OMe)_4$ requires C, 74·1; H, 7·1; OMe, 36·5%]. This 3-(3 : 4-*dimethoxyphenethyl*)-5 : 6-*dimethoxyindene* (IV), when reduced in ethanol at room temperature and pressure in presence of Adams platinum oxide catalyst, absorbed 1·04 mol. of hydrogen. The ether-soluble material was recovered and crystallised several times from methanol, giving needles (0·32 g., 5%), m. p. 81°, undepressed on admixture with 5 : 6 : 5′ : 6′-tetramethoxybis-1 : 1′-*spiro*indane (V) prepared as described above.

(ii) A similar reaction carried out over a period of 2½ hr. gave the indene (IV) (0·12 g., 1·5%), and the bis-1 : 1′-*spiro*indane (V) (3·5 g., 46%).

Cyclisation of **3-(3 : 4-*Dimethoxyphenethyl*)-5 : 6-*dimethoxyindene*** **(IV).**—(a) ***With phosphorus oxychloride.*** Cyclisation under the conditions described for the similar cyclodehydration of the ketone (III) gave the bis-1 : 1′-*spiro*indane (V) in 60% yield.

(b) ***With stannic chloride.*** The indene (2·2 g.) was dissolved in dry (K_2CO_3) chloroform (100 ml.), and stannic chloride (2 ml.) was added slowly. The green solution which gradually became bluish-purple was kept at 20° for 50 hr., then poured into 10% aqueous hydrochloric acid and ice, and shaken, and the chloroform layer and extract were separated, washed several times with dilute acid and then alkali, dried, and distilled. The residue was crystallised from a small volume of methanol at 0°, giving the spiran (V) (1·3 g., 60%), m. p. and mixed m. p. 81° (Found: C, 73·9; H, 7·1%).

5 : 6 : 5′ : 6′-*Tetrahydroxybis*-1 : 1′-spiro*indane* **(II).**—**5 : 6 : 5′ : 6′-Tetramethoxybis-1 : 1′-*spiro*indane** (V) (3 g.) was refluxed with glacial acetic acid (25 ml.) and aqueous hydrobromic acid (*d* 1·5; 25 ml.) for 5 hr., and the resulting deep-blue solution added to ice-water (500 g.) and repeatedly extracted with ether (total 300 ml.). The washed, dried extract yielded a residue which was taken up in chloroform (400 ml.), boiled with charcoal, concentrated (to 300 ml.), and kept at 0°; the resulting solid crystallised at 0° from a small volume of methanol containing a little acetic acid. The microcrystalline product had m. p. 290° and was difficult to purify. Treatment with boiling acetic anhydride and anhydrous sodium acetate for 4 hr. and addition of water gave the ***tetra-acetyl derivative*** which separated from methanol as plates, m. p. 200° [Found: C, 66·5; H, 5·5; Ac, 39·2. $C_{17}H_{12}O_4Ac_4$ requires C, 66·4; H, 5·4; Ac, 38·1%).

4 : 5 : 4′ : 5′-*Tetramethoxybenzophenone*-2 : 2′-*dicarboxylic Acid* **(VII)** ***and its*** **spiro-*Anhydride*** **(VI).**—Finely powdered **5 : 6 : 5′ : 6′-tetramethoxybis-1 : 1′-*spiro*indane** (V) (3·6 g.) was added to a stirred solution of potassium permanganate (10 g.) in water (600 ml.) on a boiling-water bath, and after 1 hr. powdered potassium permanganate was added in portions (1 g. each) until no further reaction occurred (total, 17 g. during 2 hr.). The solution was then cleared by sulphur dioxide, concentrated (to *ca.* 200 ml.), and cooled and the solid collected, washed, and dried. This product (0·77 g.) was then crystallised from 50% acetic acid giving the *spiro*-anhydride (VI) of **4 : 5 : 4′ : 5′-tetramethoxybenzophenone-2 : 2′-dicarboxylic acid** as needles, m. p. 295° [Found: C, 61·3; H, 4·5; OMe, 33·0. Calc. for $C_{15}H_4O_4(OMe)_4$: C, 61·3; H, 4·3; OMe, 33·3%], undepressed on admixture with an authentic specimen, m. p. 296°, prepared as described below. This anhydride does not dissolve in 10% aqueous sodium hydroxide.

When the anhydride (VI) (0·086 g.) was warmed with 10% ethanolic potassium hydroxide (5 ml.) the clear solution subsequently deposited needles of the crude potassium salt (0·096 g.) of the related acid. This salt when dissolved in water (2 ml.) and acidified with 10% hydrochloric acid in the cold gave a precipitate which was collected, washed with cold water, and dried ***in vacuo***, giving **4 : 5 : 4′ : 5′-*tetramethoxybenzophenone*-2 : 2′-*dicarboxylic acid*** **(VII)**, which melts at 295° after conversion into the anhydride (VI) [Found: C, 58·4; H, 5·0; OMe, 33·4%; equiv., 194. $C_{13}H_4O(OMe)_4(CO_2H)_2$ requires C, 58·5; H, 4·6; OMe, 31·8%; equiv., 195]. It dissolves readily in 10% aqueous sodium hydroxide or sodium carbonate.

spiro-*Anhydride of* 4 : 5 : 4′ : 5′-*Tetramethoxybenzophenone*-2 : 2′-*dicarboxylic Acid* **(VI).**—Difficulty was encountered in repeating the oxidation of **2 : 2′-dimethyl-4 : 5 : 4′ : 5′-tetramethoxydiphenylmethane** by the procedure described by Oliverio and Boumis.[7] The finely powdered substance (2·5 g.) was added to a stirred solution of potassium permanganate (6 g.)

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in water (250 ml.) on a boiling-water bath. After 2 hr. powdered potassium permanganate (4 g.) was added, and 2 hr. later the hot solution was filtered to remove manganese dioxide and starting material (1·5 g. recovered), then acidified with hydrochloric acid and boiled until no further precipitate was formed. This anhydride (VI) was collected, washed, dried (yield, 0·6 g., 50% after allowance for recovered material), and crystallised from 1 : 1 chloroform–methanol (16 ml.), giving needles, having m. p. 296° which could not be raised by repeated crystallisation. Oliverio and Boumis [7] record m. p. 305°; it is possible that this m. p. was corrected.

5 : 6 : 5′ : 6′-*Tetramethoxybis*-1 : 1′-spiro*indane*-3 : 3′-*dione* (VIII).—5 : 6 : 5′ : 6′-Tetramethoxybis-1 : 1′-*spiro*indane (V) (0·9 g.) was added to a solution of chromium trioxide (1·6 g.) in acetic acid (6 ml.) and water (6 ml.); after being stirred for 2 hr. and being kept for 24 hr., the mixture was poured into 10% sulphuric acid (100 ml.). The precipitated, washed solid was crystallised twice from a mixture of acetic acid (4 ml.) and methanol (1 ml.), giving the *dione* (VIII) as prisms (0·48 g., 50%), m. p. 265° [Found: C, 68·3; H, 5·6; OMe, 34·8. $C_{17}H_8O_3(OMe)_4$ requires C, 68·5; H, 5·4; OMe, 33·7%]. The *dibenzylidene derivative* was prepared in 50% yield from the dione (VIII), sodium ethoxide, and benzaldehyde in boiling ethanol (5 hr.); after addition of hydrochloric acid and evaporation, the residue was crystallised twice from methanol, giving yellow needles, m. p. 216° [Found: C, 77·1; H, 5·2; OMe, 21·8. $C_{31}H_{16}O_3(OMe)_4$ requires C, 77·2; H, 5·2; OMe, 22·8%].

Reduction of **5 : 6 : 5′ : 6′-*Tetramethoxybis*-1 : 1′-spiro*indane*-3 : 3′-*dione*** (VIII).—A mixture of the dione (VIII) (0·8 g.), amalgamated zinc (3·5 g.), concentrated hydrochloric acid (10 ml.), water (5 ml.), and acetic acid (5 ml.) was boiled for 1½ hr., then cooled, and the product crystallised from acetic acid (2 ml.) at 0°. The product, after being freed from oily material on a porous plate, separated at 0° from methanol (2 ml.) and a little light petroleum (b. p. 60—80°) in crystals (0·44 g., 60%), m. p. 80—81°, undepressed on admixture with a specimen of 5 : 6 : 5′ : 6′-tetramethoxybis-1 : 1′-*spiro*indane (V).

THE COLLEGE OF TECHNOLOGY, BRISTOL.
THE UNIVERSITY, BRISTOL.

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254. *Oxidations of Organic Compounds with Quinquevalent Vanadium. Part I. General Survey; and the Oxidation of Pinacol.*

By J. S. LITTLER and WILLIAM A. WATERS.

The susceptibility of organic compounds to oxidation by quinquevalent vanadium in sulphuric acid solution has been qualitatively surveyed. Evidence of induced polymerisation of acrylonitrile and of reduction of mercuric chloride indicates that a free-radical mechanism operates in most or all such oxidations, vanadium(v) only being reduced to vanadium(iv). The oxidation of pinacol has been studied kinetically, with a volumetric method for estimating vanadium(v). The reaction is of first-order in vanadium(v) and in pinacol, but the dependence on acidity is complex, *i.e.*, $-d[V^V]/dt = k_0[\text{Pinacol}][V^V](1 + f[H^+])$, and there is a small linear salt effect. Acrylonitrile, oxygen, and iron(iii) have no significant effect on the rate of oxidation.

THE study of the mechanisms of oxidation of organic compounds by quinquevalent vanadium has, besides its own interest, implications about the behaviour of vanadium oxide catalysts, and is of value in problems concerning possible actions of transient ions of chromium and manganese that may be concerned in certain oxidations by both chromic acid and potassium permanganate.[1] The subject was cursorily surveyed by Morette and Gaudefroy [2] primarily from an analytical viewpoint; but kinetic investigation has not extended beyond Bobtelsky and Glasner's study of oxidations of oxalic acid, formaldehyde, and ethanol.[3]

[1] W. A. Waters, *Quart. Rev.*, 1958, **12**, 277.
[2] Morette and Gaudefroy, *Bull. Soc. chim. France*, 1954, 956.
[3] Bobtelsky and Glasner, *J. Amer. Chem. Soc.*, 1942, **64**, 1462.

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Table 1.

Substrate	Oxidation test	Polymerisation test	Mercuric chloride test
Acids			
Formic	O	—	—
Acetic	O	—	—
Succinic	O	—	—
Malonic	M	—	—
Ethylmalonic	M	C	—
Diethylmalonic	O	—	—
Phenylacetic	SS	S	—
Oxalic	S	SS	O
Crotonic	O	—	—
Hex-2-enoic	M	S	—
Fumaric	O	—	—
Maleic	SS	S	SS
Lactic	F	S	SS
Glycollic	F	S	—
Tartaric	F	S	A
β-Hydroxybutyric	MB	S	—
Pyruvic	FF	SS	S
Glycine, leucine	O[SS]	—	—
Aldehydes			
Formaldehyde	S	S	A
Acetaldehyde	FB	S	—
Chloral (hydrate)	O[SS]	—	—
Propaldehyde	F	C	A
Butyraldehyde	F	C	C
Crotonaldehyde	F	C(G)	—
Ketones			
Acetone	M	C	S
Ethyl methyl ketone	F	S	S
Diethyl ketone	F	S	SS
Diisopropyl ketone	F	S	—
*cyclo*Pentanone	F	S	C
*cyclo*Hexanone	FD	C	—
Methyl*cyclo*hexanone	M	C	—
*cyclo*Heptanone	SD	C	—
Acetonylacetone	F	C	—
Diacetyl	FF	C	A
Alcohols			
Methanol	SB	C	SS
Ethanol	SB	C	—
Butan-1-ol	SB	C	—
Propan-2-ol	SB	C	—
*cyclo*Hexanol	SB	S	—
tert.-Butyl alcohol	OB[OB]H	—	—
Benzyl alcohol	SB	—	—
Ethylene glycol	SB	S	SS
1 : 2-Butylene glycol	FB	S	—
2 : 3-Butylene glycol	F	C	—
Pinacol	F	C	C
*cis-cyclo*Hexane-1 : 2-diol	FB	C	—
Alcohols			
*trans-cyclo*Hexane-1 : 2-diol	FB	C	—
1 : 2-Dimethyl*cyclo*hexane-*trans*-1 : 2-diol	F	S	—
1 : 2-Dimethyl*cyclo*pentane-*trans*-1 : 2-diol	F	C	—
Glycerol	FB	S	S
Sorbitol	FB	S	—
Mannitol	MB	C	SS
Methyl α-D-glucoside	SB	SS	—
Methyl α-D-mannoside	SB	S	—
1 : 3-Butanediol	MB	S	—
Pentaerythritol	SB	S	—
Sucrose	FB	S	SS
Phenols			
Phenol	F	SS	—
Quinol	F	—	—
1 : 4-Dihydroxynaphthalene	F	S	—
Olefins			
Oct-1-ene	FB	CG	S
*cyclo*Hexene	FB	CG	—
1 : 2-Dimethyl*cyclo*hexene	S	S	—
1 : 2-Dimethyl*cyclo*pentene	FB	CG	—
2 : 4 : 4-Trimethylpentene	FB	C	—
Styrene	SS[S]B	—	—
Stilbene	[SS]	—	—
Triphenylethylene	O	—	—
Acrylonitrile	O	O	—
Methyl methacrylate	O	O	—
Ethers, etc.			
Diethyl ether	O	—	—
Dioxan	S	SS	—
Dibenzyl ether	M	—	—
tert.-Butyl hydroperoxide	FB	—	—
Di-*tert.*-butyl peroxide	O	—	—
Nitrogen compounds			
Aniline	FF	—	—
Ethylamine	S	—	—
Diethylamine	S	SS	—
Triethylamine	M	—	—
Ethylenediamine	S	SS	S
2-Hydroxyethylamine	S	SS	S
NN-Dimethylaniline	FF.B	—	—
Acetamide	O	—	—
Nitromethane	S[M]	—	—

Oxidation Test.—O = No reaction, SS = reaction very slow even on warming, S = reaction easy on warming, M = reaction slow in cold, F = reaction easy in cold, FF = reaction very rapid in cold, B = initial red or brown colour, possibly due to complex formation when substrate contains hydroxyl groups, or to the V^V hydroperoxide colour when traces of hydroperoxide may be present, H = oxidation occurred after standing for one month, D = red product formed during oxidation when ketone is in excess, [ ] = reaction carried out with 0·4N-V^V in 8N-H_2SO_4. Other reactions used 0·2N-V^V in 5N-H_2SO_4.

Polymerisation Test.—O = No polymerisation, SS = very slight cloudiness, S = definite cloudiness, C = thick polymer, G = test material polymerises itself. In no case did polymer appear before the initial red or brown colour, if any, had disappeared.

Mercuric Chloride Test.—SS = Very slight precipitate, S = slight precipitate, A = appreciable precipitate, C = considerable precipitate, O = no formation of mercurous chloride.

Oxidations involving vanadium(v) in solution are acid-dependent and due to a cationic form of vanadium, usually regarded as VO_2^+ aq.,[4] which forms bright yellow solutions in acidities over pH 1·5. Since both vanadic and vanadous salts are strong reducing agents the organic oxidations effected by vanadium(v) (pervanadyl) solutions proceed to the end-point of the blue vanadyl salt (V^{IV}), but every oxidation is not necessarily due to the one-electron transition $V^V \longrightarrow V^{IV}$. The alternative sequence $2e + V^V \longrightarrow V^{III}$ (slow); $V^{III} + V^V \longrightarrow 2V^{IV}$ (fast) has been suggested for certain inorganic oxidations.[3, 5]

In a preliminary survey (Table 1) we have used the two tests employed by Drummond and Waters [6] to characterise the oxidations effected by manganese(III), *viz.*, (*a*) induced polymerisation of vinyl cyanide and (*b*) induced reduction of mercuric chloride. Positive evidence of radical formation during the oxidations of aldehydes, ketones, α-hydroxy-acids, and some 1 : 2-glycols was obtained by both tests; with other compounds, *e.g.*, alcohols and olefins, catalysis of polymerisation occurs though the mercuric chloride test is not conclusive. In particular the oxidation of oxalic acid fails to induce the reduction of mercuric chloride, although the precipitate of mercurous chloride might be expected [6] to be especially copious in this instance. The often inconclusive nature of the mercuric chloride test does not disprove the presence of radicals, for it appears (see below) that vanadium(v) can react very rapidly with any radicals present, and so prevent their reduction of mercuric chloride. The polymerisation test certainly indicates that oxidations with vanadium(v) generally proceed by one-electron transitions, for vanadium-(IV) and -(III) could not initiate polymerisation under the conditions used, although the latter could do so in the presence of oxygen. However it would be premature to infer that all reactions involving reduction of vanadium(v) to vanadium(IV) by organic materials proceed by one-electron mechanisms. We propose to make a systematic survey of these reactions.

Our first example, the oxidation of pinacol, which we have already studied in detail, does however provide a clear example of a one-electron transfer process. We have found that (1) the reaction is quantitative according to the equation

$$(\cdot CMe_2 \cdot OH)_2 + 2V^V = 2Me_2CO + 2V^{IV} + 2H^+$$

(2) it does catalyse the polymerisation of vinyl cyanide, and (3) it does produce radicals which can effect the reduction of mercuric chloride to mercurous chloride, but do not absorb free oxygen.

A kinetic study of this oxidation has been made by use of Morette and Gaudefroy's titrimetric procedure,[2] which, in daylight, proved to be more rapid and reliable at low concentrations than electrometric titration. Solutions of sodium or ammonium vanadate in aqueous sulphuric acid were used as the oxidiser, and, by the method of independent variation of both [pinacol] and [V^V], the reaction was shown to be of first order in vanadium up to 85% completion at least and also of first order in pinacol, as Tables 2 and 3 show.

Though vanadium(v) is amphoteric, it exists only as a cation in solutions of acidity greater than 0·05M. In sulphuric acid between 0·3M and 0·75M the rate of oxidation is independent of the acidity (Table 4) within experimental error, and shows a linear positive salt effect (Table 5) indicating that the rate-determining reaction is taking place between a neutral molecule and an ion.

[4] LaSalle and Cobble, *J. Phys. Chem.*, 1955, **59**, 119.

[5] Ramsey, Colichman, and Pack, *J. Amer. Chem. Soc.*, 1946, **68**, 1695; Boyer and Ramsey, *ibid*, 1953, **75**, 3802; Kirson and Bobtelsky, *Bull. Soc. chim. France*, 1947, 560; Bobtelsky and Czosnek, *Z. anorg. Chem.*, 1932, **205**, 401; **206**, 113; Krauze and Vorob'eva, *Sci. Rep. Moscow State University*, 1936, **6**, 5; Higginson, Sutton, and Wright, *J.*, 1953, 1380; 1402; Trujillo and Rios, *Anales real. Soc. espan. Fis. Quim.*, 1954, **49**, *B*, 473.

[6] Drummond and Waters, *J.*, 1953, 2836, 3119.

TABLE 2.

Dependence of rate on $[V^V]$ *at 25·0°.*

[Pinacol] = 0·0968M.

$[H_2SO_4]$ (M)	$[V^V]$initial (N)	10^4k (sec.$^{-1}$)
0·375	0·0099	2·31
0·425	0·0197	2·26
0·5	0·0495	2·36
0·75	0·0987	2·41

Mean value of $k = (2{\cdot}34 \pm 0{\cdot}05) \times 10^{-4}$ sec.$^{-1}$.

Individual experiments showed no significant departure from first-order kinetics up to 85% completion.

TABLE 3.

Dependence of rate on [Pinacol] at 25·0°

[Pinacol] (M)	10^4k	10^4k/[Pinacol]
0·0268	0·649	2·42
0·0535	1·18	2·21
0·0968	2·26	2·33
0·1775	4·49	2·53
0·2785	7·45	2·67
0·1135	2·75	2·42

Mean value of k/[Pinacol] = $(2{\cdot}43 \pm 0{\cdot}14) \times 10^{-3}$ mole^{-1} sec.$^{-1}$.

All experiments except the last were carried out in 0·35M-acid, with $[V^V] = 0{\cdot}02$N and an atmosphere of air. The last was in 0·5M-acid with $[V^V] = 0{\cdot}05$N and an atmosphere of nitrogen.

TABLE 4. *Dependence of rate on* $[H^+]$ *at low acidities at 25·0°.*

$[V^V] = 0{\cdot}0494$N, [Pinacol] = 0·0968M.

$[H_2SO_4]$ (M)	0·3	0·375	0·5	0·75
10^4k	2·31	2·22	2·36	2·43

Mean value of $k = (2{\cdot}33 \pm 0{\cdot}11) \times 10^{-4}$ sec.$^{-1}$.

TABLE 5. *Dependence of rate on ionic strength at 30·0°.*

[Pinacol] = 0·032M, $[V^V] = 0{\cdot}0241$N, $[H_2SO_4] = 0{\cdot}25$M.

Ionic strength (M)	0·83	1·42	2·0
10^4k (sec.$^{-1}$)	1·4	1·63	1·91

The added salt was sodium chloride. Extrapolation gives $k = 1{\cdot}07 \times 10^{-4}$ sec.$^{-1}$ at zero ionic strength.

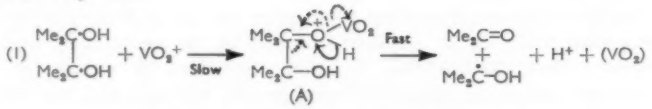
TABLE 6. *Dependence of rate on [Acrylonitrile] at 25° in nitrogen.*

[Pinacol] = 0·1135M, [Acid] = 0·5M, $[V^V] = 0{\cdot}050$N.

[Acrylonitrile] (M)	0·0	0·062	0·157	0·470	2·82
10^4k (sec.$^{-1}$)	2·75	2·96	2·82	2·92	3·55

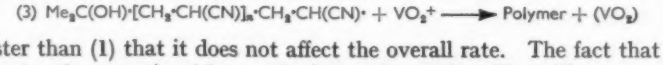
The presence of polymer did not appear to affect the sampling technique or the accuracy of the titrations.

The foregoing information accords with the following mechanism, where (A) may be an irreversibly formed compound or transition complex, and (VO_2) is the basic oxide of the eventual vanadyl salt:



(A)

Now the oxidation of pinacol by manganic pyrophosphate [6] was retarded by the addition of vinyl cyanide, but, as Table 6 shows, the addition of vinyl cyanide has very little effect on the rate of oxidation of pinacol by vanadium(v), although a polymer containing hydroxyl groups is formed. Consequently the oxidation of the polymer radical (3) must be



so much faster than (1) that it does not affect the overall rate. The fact that polymer is formed indicates that reaction (4) must be faster than either (2) or (3).

In solutions of high sulphuric acid concentration however the oxidation is not so simple as eqns. (1) and (2) indicate, for the rate of reactions markedly increases at high

acidities, as Table 7 and Fig. 1 show. H_0 was obtained from the figures of Paul and Long,[7] and $\alpha_\pm$ from the figures of Stokes.[8] k_0 was found to be $1{\cdot}31 \times 10^{-4}$ sec.$^{-1}$. Sulphuric acid can be assumed to be a strong, monobasic acid throughout this range.

TABLE 7. *Dependence of rate on acid concentration over an extended range of acidity at 30°.*

[Pinacol] = 0·032M, [V^V] = 0·0241N.

[H_3O^+] (M)	0·05	0·25	1·2	2·15	3·05	4·0	4·95	5·85
H_0	1·0	0·44	−0·38	−0·93	−1·40	−1·85	−2·26	−2·68
$a \pm$	0·015	0·0495	0·154	0·278	0·436	0·68	1·02	1·46
10^4k (sec.$^{-1}$)	1·33	1·40	1·90	3·10	6·08	12·0	19·6	35·0

To elucidate this effect of strong acid the oxidation rate has been plotted against various acidity functions. Also the total rate constant k has been divided into two portions, k_0, a hydrogen-independent value obtained by extrapolating the measured rate to $[H_3O^+] = 0$, and k_1, an acid-dependent portion, such that $k = k_0 + k_1$; these have also been plotted against acidity functions (Figs. 1—4).

FIG. 1. *Dependence of the rate of the reaction of vanadium*(V) *with pinacol on acidity.*

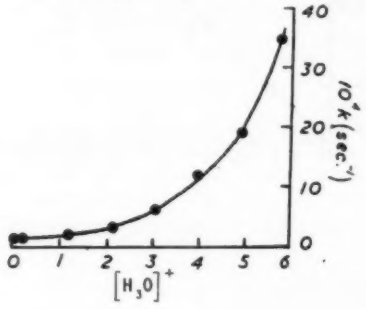
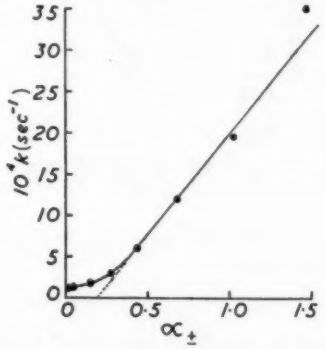


FIG. 2. *Dependence of the rate of the reaction of vanadium*(V) *with pinacol on the total activity of the acid, $a_\pm$.*



Potentiometric determinations of hydrogen-ion activity, a_{H^+}, in solutions identical with the reaction mixtures except for the omission of the organic substrate, a glass electrode and a calomel electrode being used, gave a curve very similar to that obtained when the mean activity of the acid ($\alpha_\pm$) is used (Fig. 2). The significance of such a_{H^+} measurements is, however, not great in solutions of the acidities used, and $\alpha_\pm$, though exact, is a mean function of both H_3O^+ and HSO_4^- ions. However the curve appears to be approximately linear in regions where the acid dependent reaction is most important.

Fig. 3 illustrates that the dependence of k_1 on total acid concentration [H_3O^+] is approximately of first order at the lower acidities, but the line has a positive curvature, and at high acidities is of second or higher order. Fig. 4 shows that if the Hammett function, H_0, is the relevant acidity function to correlate with log k_1 then a good first-order plot is obtained over a wide acidity range, but at really high acid concentrations the rate increases more slowly than direct proportionality requires.

To a first approximation the acid-dependence of the reaction can be explained by postulating the existence of an equilibrium (5), as suggested by Ramsey, Colichman, and Pack,[5]

$$(5)\quad VO_2^+ + H^+ \underset{}{\overset{K}{\rightleftharpoons}} VO_2H^{2+}$$

[7] Paul and Long, *Chem. Rev.*, 1957, **57**, 1.
[8] Stokes, *Trans. Faraday Soc.*, 1948, **44**, 295.

followed by (6):

$$(6)\ VO_2H^{2+} + \text{Pinacol} \xrightarrow{\text{Slow}} \text{Complex} \xrightarrow{\text{Fast}} \text{Products} + (VO_2)$$

the attack of the doubly charged cation which is a more powerful oxidiser than VO_2^+. When this is taken into account the rate equation for the acid-dependent reaction becomes

$$\frac{-d[V^V]}{dt} = \frac{k'K[V^V][H^+][\text{Pinacol}]}{1 + K[H^+]}$$

where $k'K = k_1$.

If $K \approx 1/[H^+]$ then a falling off from first-order dependence will result. This law can explain dependence on either $[H_3O^+]$ or the Hammett function h_0, for dependence on h_0

FIG. 3. *Graphical determination of the order of the reaction of vanadium(v) with pinacol with respect to acid concentration. Curve A refers to total rate (k), curve B to acid-dependent rate (k_1).*

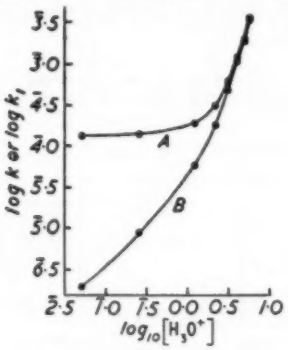
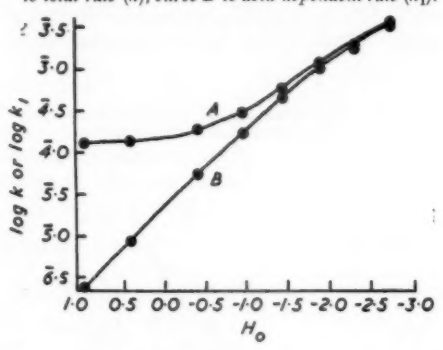


FIG. 4. *Graphical determination of the order of the reaction of vanadium(v) with pinacol with respect to the Hammett acidity function. Curve A refers to total rate (k), curve B to acid-dependent rate (k_1).*



could be consistent with eqn. (5), and dependence on $[H_3O^+]$ would not be inconsistent with eqn. (5A):

$$(5A)\ VO_2^+ + H_3O^+ \overset{K}{\rightleftharpoons} V(OH)_3^{2+}$$

followed by attack on pinacol by $V(OH)_3^{2+}$.

In theory, the Hammett function h_0 is not the correct acidity function for use in connection with equilibrium (5), and it should be replaced by h_+, which is appropriate for addition of a proton to a cation. However values of H_+ are not available in strong sulphuric acid, and Bonner and Lockhart have shown [9] that in certain ranges H_0 and H_+ change in a parallel manner.

An alternative explanation of the acidity dependence at high acidity may however be adduced from the observation that as the strength of the acid is increased the colour of the vanadium(v) solution changes gradually from yellow to deep red. If this is due to a sulphate complex [10] then the curvature of either Fig. 3 or 4 could be accounted for, by suggesting (*a*) that the primary dependence is on $[H_3O^+]$ and that sulphate complex is a more powerful oxidising agent than the VO_2H^{2+} or $V(OH)_3^{2+}$ which it replaces, or (*b*) that the primary dependence is on h_0 and that the sulphate complex is a less powerful oxidiser. Salt effects may also affect the form of the dependence on acidity, for no attempt was made to keep the ionic strength constant.

Thus the observed kinetics accord with the equation

$$-d[V^V]/dt = k_0[V^V][\text{Pinacol}]\{1 + f([H^+])\}$$

where the precise reason for the form of $f([H^+])$ has not yet been established.

[9] Bonner and Lockhart, *J.*, 1957, 364.
[10] Ducret, *Ann. Chim.* (*France*), 1951, **6**, 705.

Experimental

Qualitative Tests (*Table* 1).—Oxidation tests were carried out by adding an excess of the substance to a solution of vanadium(v) in sulphuric acid. Reduction of the vanadium to the blue of vanadium(IV) *via* green was observed visually.

Polymerisation Tests.—Acrylonitrile and the substrate were placed in the lower part of a Thunberg tube while vanadium(v) solution was placed in the top part. The tubes were evacuated, filled with pure dry nitrogen twice, and then evacuated again. If after 30 min. no polymer had formed the liquids were mixed, and, if necessary, warmed to 70° to accelerate oxidation. If polymer tended to form as a result of distillation within the tube, the latter was left filled with nitrogen. Every experiment was accompanied by a blank control.

Mercuric Chloride Test.—The substrate, saturated mercuric chloride solution, and vanadium(v) solution were mixed in a test-tube and examined after 18 hr. Only small quantities of a white precipitate of mercurous chloride were ever observed and the test was often obscured by cloudiness resulting from the oxidation. In a few cases the nature of the precipitate was confirmed by separating it and showing that it was blackened by ammonia.

Except for the olefins, all the substances listed are wholly or partially miscible with water, and so these oxidations are not controlled by solubility limitations. With the olefins, however, the rate is probably solubility-controlled. The oxidation of amines is noticeably acid-dependent, being stopped when the acid is too concentrated. Since acid concentrations were not carefully controlled, the relative rates of oxidation of the various amines has not definitely been established.

The possibility that vanadium-(III) or -(IV) might be able to initiate polymerisation was investigated by mixing a suitably reduced sample of the stock solution of vanadium with acrylonitrile. Neither valency state was capable of causing polymerisation in the absence of air, but if air was admitted to solutions containing V^{III} or mixtures of V^{III} and V^{IV} then a surface film of polymer formed. Uptake of oxygen by V^{III} solutions in the absence of monomer was confirmed by the Warburg technique. Dainton and James's [11] report on similar experiments is not entirely clear, but if in fact these investigators have found that solutions of V^{III} did not form a reduction–activation system with oxygen, then the discrepancy may perhaps be due to the greater acidity of the solutions used in the present work.

Materials.—Vanadium(v) *solutions.* For the qualitative work commercial sodium orthovanadate was dissolved or suspended in water and the calculated quantity of concentrated acid added. For the kinetic work B.D.H. Laboratory Reagent grade sodium metavanadate was used. " AnalaR " ferrous ammonium sulphate was used to prepare a standard solution against which the vanadium(v) solution was titrated. Acrylonitrile, freed from inhibitor by washing with alkali and water, was dried, and distilled under nitrogen. Pinacol was distilled, then recrystallised four times from distilled water. It was used as the dry hexahydrate, m. p. 46·5°.

Kinetic Measurements.—The reactions were carried out in a thermostat regulated to within ±0·05°. After measured time intervals, from 8 to 10 aliquot portions of reaction mixtures, which usually contained a large excess of one component, were each added in succession to a known excess of ferrous solution, and the excess of Fe^{2+} was titrated with V^{V} solution, barium diphenylaminesulphonate in the presence of phosphoric acid being used as indicator. The apparent rate constants were then evaluated from log $[V^{V}]$–time plots. When acrylonitrile was present the solutions were blown out with pure dry nitrogen before mixing, and nitrogen was passed through them during the reaction. Comparison of an experiment conducted under nitrogen with ones open to the air (see Table 3) indicated that oxygen was not interfering, and the absence of any oxygen uptake was confirmed by the Warburg technique.[12] No catalytic effect was detected when 0·0099M-ferric alum was present.

Investigation of Stoicheiometry.—A weighed sample of pinacol was oxidised overnight by a known excess of vanadium(v) solution and the remaining oxidant was then estimated. 1 mole of pinacol required 2·04 ± 0·03 equivalents of vanadium(v). After reduction of the excess of vanadium(v), 2 : 4-dinitrophenylhydrazine was added to the solution and acetone 2 : 4-dinitrophenylhydrazone, m. p. 128° (and mixed m. p. with an authentic specimen), was collected in 102% yield.

Dyson Perrins Laboratory, Oxford. [*Received, November 5th*, 1958.]

[11] Dainton and James, *Trans. Faraday Soc.*, 1958, **54**, 649.
[12] Milton and Waters, " Methods of Qualitative Microanalysis," Arnold, London, 1949, pp. 562—573.

XUM

255. *Use of Cobalt Catalyst in the Preparation of Borazole and its Derivatives.*[1]

By H. J. Emeléus and G. J. Videla.

Brown and Laubengayer [2] described the preparation of *B*-trichloroborazole by passing boron trichloride vapour with nitrogen over ammonium chloride at 165—175°, or by refluxing chlorobenzene in which ammonium chloride was suspended, while boron trichloride vapour was passed in. Both procedures gave yields of about 35%. In using the first of these methods we found that the yield was only 10—12% when ammonium chloride of A.R. purity was used, whereas the salt of commercial purity gave yields of about 30%. As the latter contained ferric chloride, we were led to study metallic iron, cobalt, and nickel as catalysts for the preparation of *B*-trichloroborazole and *B*-trichloro- and *B*-tribromo-*N*-trimethylborazole. Preliminary results show that the best results were obtained with cobalt, which was examined in some detail.

The catalyst was prepared by reducing cobalt oxide on a pumice support and the product was mixed with ammonium chloride in a 1 : 10 ratio. With ammonium chloride and boron trichloride a smooth reaction occurred at 80—120° when Brown and Laubengayer's general procedure was followed, and the amount of non-volatile product was reduced, probably because of the lower temperature. With methylamine hydrochloride in place of ammonium chloride, reaction was complete at 150° and yields were similar. Even more striking results were obtained in preparing *N*-tribromoborazole from ammonium bromide and boron tribromide. Without catalyst, reaction occurred at 280—290° and the yield was very low, whereas, with catalyst, there was a smooth reaction at 160—180° and a yield of purified product of 40—45%. Results with methylamine hydrobromide were similar. When hydrazine salts were used in place of those of ammonia the reaction temperature was reduced, even without the use of a catalyst. Thus hydrazine hydrochloride reacted with boron trichloride at 80—120° and gave a 35% yield of purified trichloroborazole: with catalyst, the reaction temperature was 80° and the yield about 50%. Results for hydrazine hydrobromide and boron tribromide were similar. With methylhydrazine hydrobromide and boron tribromide reaction was complete at 150° and the yield of purified *B*-tribromo-*N*-trimethylborazole was 45%: without catalyst these values were 160—180° and 6—8% respectively.

Hydrazine salts also give enhanced yields in the preparation of borazole by the method of Schaeffer, Schaeffer, and Schlesinger,[3] who showed that ammonium chloride and lithium borohydride gave yield of borazole of about 30% at 290°, whilst reaction did not occur with sodium borohydride. On use of hydrazine hydrochloride, borazole was formed with lithium or sodium borohydrides at 180° in 40—50% yield. The cobalt catalyst was used in the case of the sodium salt. Further experiments are being made to elucidate the mode of action of the cobalt, which is probably converted superficially into chloride. Though its effect on these reactions is not equally great in each instance, it is sufficiently striking to suggest that its presence facilitates the formation of one of the intermediates in the poorly understood reactions which result in borazole and its derivatives. We hope also to examine other possible catalysts.

Experimental.—Preparations were done in a long combustion tube heated near the inlet end, in which the salt was placed, by a small electric furnace as described by Brown and Laubengayer.[2] The boron halide (8—15 g. per hr.) was passed over the salt mixed with catalyst, which was prepared by damping powdered pumice (30 g.) with saturated cobalt nitrate solution, drying, and calcining at 800—850°. The product was reduced in hydrogen at 300—350°. The catalyst (3—4 g.) was ground with the halide (30 g.) in a dry box.

Preparation of trichloroborazole. Ammonium chloride (30 g.), mixed with catalyst (3—4 g.),

[1] See Emeléus and Videla, *Proc. Chem. Soc.*, 1957, 288.
[2] Brown and Laubengayer, *J. Amer. Chem. Soc.*, 1955, **77**, 3699.
[3] G. Schaeffer, A. Schaeffer, and Schlesinger, *ibid.*, 1951, **73**, 1612.

was placed in the heated zone of the reaction tube and boron trichloride vapour mixed with nitrogen was passed at a controlled rate. Reaction commenced at 80° and was complete below 120°. Crude product was removed from the cold part of the tube in a dry box and purified by vacuum sublimation at 70° (yield 20·5 g., 60% on ammonium chloride taken) (Found: B, 17·6; Cl, 57·9; N, 22·8. Calc. for $B_3N_3H_3Cl_3$: B, 17·7; Cl, 57·6; N, 22·8%); m. p. 84° (sealed tube). The vapour pressures agreed with values reported by Brown and Laubengayer. The infrared spectrum, which will be reported elsewhere, showed no B–H frequency.

Preparation of B-*trichloro*-N-*trimethylborazole*. Dry methylamine hydrochloride (25 g.), mixed with catalyst (2·5 g.), was treated as above. Reaction started at 100° and was complete at 150°. The crude product was sublimed *in vacuo* at 120° (yield 6·8 g., 50% on methylamine hydrochloride taken) (Found: B, 14·3; N, 18·5; C, 15·8; H, 4·2%; *M*, cryoscopic in benzene, 225. Calc. for $C_3H_9B_3N_3Cl_3$: B, 14·4; N, 18·6; C, 16·0; H, 4·0%; *M*, 226).

Preparation of B-*tribromoborazole*. Ammonium bromide (10 g.) was mixed in a dry box with cobalt catalyst (1 g.). Reaction with boron tribromide carried in nitrogen commenced at 160° and was complete at 200°. The crude product was sublimed *in vacuo* at 120° (yield 8·2 g., 42% on ammonium bromide taken) (Found: B, 10·0; Br, 74. Calc. for $B_3N_3H_3Br_3$: B, 10·2; Br, 75·6%); m. p. 128—129° (sealed tube).

Preparation of B-*tribromo*-N-*trimethylborazole*. Methylamine hydrobromide (18 g.) was mixed with catalyst (1·8 g.). Reaction with boron tribromide carried in nitrogen started at 190° and was complete at 220°. The crude product was sublimed at 120° (yield 5·6 g., 40% on methylamine hydrobromide taken) (Found: B, 8·95; N, 11·3; Br, 66·4; C, 9·7%; *M*, cryoscopic in benzene, 358. Calc. for $C_3H_9B_3N_3Br_3$: B, 9·05; N, 11·6; Br, 66·75; C, 10·0%; *M*, 359).

Preparation of B-*trichloroborazole from hydrazine hydrochloride*. The procedure was the same as with ammonium chloride. Hydrazine hydrochloride (25 g., dried *in vacuo* over P_2O_5) was placed in the heated tube and boron trichloride (38 g., 19 g. per hour) was passed in at 120°. The crude product was sublimed in *vacuo* at 70° (yield 6·90 g., 35% on hydrazine hydrochloride taken). The same quantities of reactants being used with the addition of 10% of catalyst, reaction was complete at 120° (yield of sublimed trichloroborazole, 9·7 g., 50%). In both cases, and in the experiments described below, the purity of the product was controlled by analysis, m. p., and infrared spectrum.

Preparation of B-*trichloro*-N-*trimethylborazole with methylhydrazine hydrochloride*. The hydrazine hydrochloride (25 g.) was treated as above with boron trichloride (26 g., 13 g./hr.). Reaction started at 120° and the temperature was raised to 140° for the last 20 min. The yield of sublimed *B*-trichloro-*N*-trimethylborazole was 5·72 g. (30%). With the same quantities and procedure, but with 10% of cobalt catalyst, reaction occurred at 110°, the yield of pure product was 7·1 g. (45%).

Preparation of B-*tribromoborazole with hydrazine hydrobromide*. Hydrazine hydrobromide (11·6 g.) was treated as above with boron tribromide (16 g. in 2 hr.). Reaction was complete at 180°. The yield of pure product was 1·9 g. (30%). With the same quantities but with the addition of 10% of cobalt catalyst, the yield was 2·5 g. (40%).

Preparation of B-*tribromo*-N-*trimethylborazole with methylhydrazine hydrobromide*. Methylhydrazine hydrobromide (12·3 g.) was treated with boron tribromide (16 g. in 2 hr.) at 160—180°. The yield of pure sublimed product was 0·6 g. (8%). With the same quantities, but with the addition of 10% of cobalt catalyst, reaction was complete in 2 hr. at 140—150°. The yield of sublimed product was 2·52 g. (45%).

Preparation of borazole by use of lithium and sodium borohydride. In a typical experiment hydrazine hydrochloride (10·5 g.) (dried in *vacuo* over P_2O_5) was mixed with crushed Pyrex glass (30 g.) in a dry box and transferred to the reaction flask, which was swept out with dry nitrogen. Lithium borohydride (4·35 g.) was added and the contents were mixed. The flask was attached to cooled traps and the usual vacuum fractionation apparatus and heated at 175—180° until hydrogen evolution ceased (1½ hr.). The volatile products were collected and fractionated. The borazole (3·8 g., 50%) was characterised by vapour-pressure measurements and by its m. p. and infrared spectrum. By the same procedure but with sodium borohydride (11·3 g.), hydrazine hydrochloride (10·5 g.), and cobalt catalyst (1·2 g.) the yield of pure borazole was 3·18 g. (40%).

One of the authors (G. J. V.) thanks the Argentine Atomic Commission for Study Leave.

UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, August 27th*, 1958.]

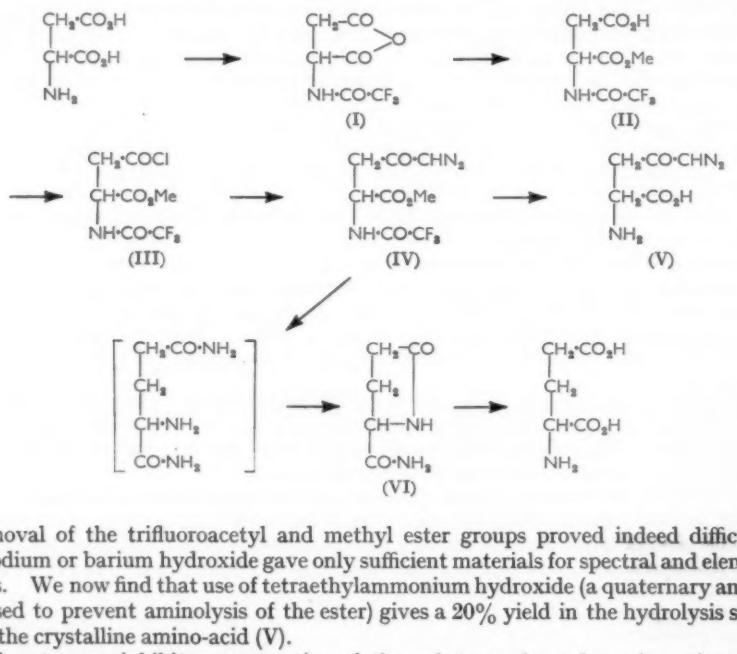
XUM

256. *Synthesis of 5-Diazo-4-oxo-L-norvaline.*

By Y. Liwschitz, R. D. Irsay, and A. I. Vincze.

6-Diazo-5-oxo-L-norleucine (DON) has antibiotic and tumour-inhibitory properties.[1] Since, moreover, Mickelson and Flippen [2] showed that hydrolysates of tumorous mouse tissue (Sarcoma 180) contained significantly less aspartic acid than that of healthy animals, it appeared of interest to prepare the lower homologue, 5-diazo-4-oxo-L-norvaline, related to aspartic acid.

Our synthesis [3] of this substance (summarised in the scheme) is based on the α-methyl ester of *N*-trifluoroacetyl-L-aspartic acid. Weygand and his co-workers independently prepared 5-diazo-4-oxo-*N*-trifluoroacetyl-L-norvaline ethyl ester by the same route [4] but failed to remove the protecting groups in this particular instance, although they succeeded in synthesising two higher homologues, *i.e.*, 6-diazo-5-oxo-L-norleucine and L-2-amino-7-diazo-6-oxoœnanthic acid.[5] Our previous attempts to prepare the substance by catalytic hydrogenation of *N*-benzyloxycarbonyl-5-diazo-4-oxo-L-norvaline benzyl ester were unsuccessful, since the diazo-group was affected, in accordance with the findings of others.[6]



Removal of the trifluoroacetyl and methyl ester groups proved indeed difficult and using sodium or barium hydroxide gave only sufficient materials for spectral and elementary analysis. We now find that use of tetraethylammonium hydroxide (a quaternary amine has to be used to prevent aminolysis of the ester) gives a 20% yield in the hydrolysis step and affords the crystalline amino-acid (V).

So far, tumour-inhibitory properties of the substance have been investigated only against Sarcoma 37 in mice: administration of 8—10 mg./kg. reduced tumour sizes by 26·4% (average), and the substance is thus "intermediate" in the nomenclature of the American Association for Cancer Research.

[1] Dion, Fusari, Jakubowski, Zora, and Bartz, *J. Amer. Chem. Soc.*, 1956, **78**, 3075.
[2] Mickelson and Flippen, *Archiv. Biochem. Biophys.*, 1956, **64**, 246.
[3] For a preliminary announcement to the Israel Chemical Society, April, 1957, see Liwschitz and Irsay, *Bull. Res. Council Israel*, 1957, **6**, 292.
[4] Weygand, Klinke, and Eigen, *Chem. Ber.*, 1957, **90**, 1896.
[5] Weygand, Bestmann, and Klieger, *ibid.*, 1958, **91**, 1037.
[6] Wienhaus and Ziehl, *Ber.*, 1932, **65**, 1461; Birkofer, *Chem. Ber.*, 1947, **80**, 83.

Experimental.—M. p.s were determined in a Fisher–Johns apparatus. Biological tests were carried out by Dr. M. Schlesinger of the Dept. of Experimental Pathology (Cancer Research Laboratories), The Hebrew University, Hadassah Medical School, Jerusalem, whose help is greatly appreciated.

α-*Methyl hydrogen* N-*trifluoroacetyl*-L-*aspartate* (II). *N*-Trifluoracetyl-L-aspartic anhydride [4] (13 g.) was heated under reflux with absolute methanol (50 ml.) for 4 hr. After removal of the solvent *in vacuo*, the residue solidified overnight to a pasty mass. Recrystallisation from a small volume of chloroform and prolonged cooling yielded prisms, m. p. 114—115° (11·5 g., 77%), of the *ester* (Found: C, 35·0; H, 3·5; N, 5·8. $C_7H_8O_5NF_3$ requires C, 34·6; H, 3·3; N, 5·8%), $[\alpha]_D^{21}$ −13·6° (*c* 0·22 in ethyl acetate).

L-β-*Methoxycarbonyl*-β-*trifluoroacetamidopropionyl chloride* (III). The ester (II) (7 g.) and thionyl chloride (2·5 ml.) were refluxed in benzene (30 ml.) for 30 min. After removal of the solvent and excess of reagent *in vacuo*, the residue solidified. Recrystallisation from benzene gave the *chloride* as needles, m. p. 127° (7·1 g., 94%). Further recrystallisation from benzene raised the m. p. to 128° (Found: N, 5·2; Cl, 13·3. $C_7H_7O_4NClF_3$ requires N, 5·3; Cl, 13·6%). $[\alpha]_D^{24}$ was −17·4° (*c* 0·23 in ethyl acetate).

5-*Diazo*-4-*oxo*-N-*trifluoroacetyl*-L-*norvaline methyl ester* (IV). Freshly prepared chloride (III) (6·5 g.) in dry ether (20 ml.) was added with stirring to ethereal diazomethane (large excess) at 0°. After 10 min. the mixture was freed from a small amount of solid, and excess of reagent and solvent were removed *in vacuo*. The residual *ester* recrystallised from benzene as long yellow needles, m. p. 113—114° (5 g., 76%) (Found: C, 36·3; H, 3·3; N, 14·0. $C_8H_8O_4N_3F_3$ requires C, 36·0; H, 3·0; N, 15·7%. Nitrogen determinations of aliphatic diazo-compounds tend to be low), $[\alpha]_D^{15}$ −11·3° (*c* 0·167 in methanol).

Glutamic acid by Wolff rearrangement and hydrolysis of the ester (IV). The ester (0·5 g.) in dioxan (10 ml.) was slowly added to a mixture of sodium carbonate (0·125 g.), silver oxide (0·05 g.) and sodium thiosulphate (0·075 g.) in 5 ml. of water at 50—60°. After 90 min., during which the temperature was gradually raised to 100°, part of the yellow diazoketone still remained. The mixture was refluxed for 3 hr., then evaporated *in vacuo*. The residue was heated under reflux with 20% hydrochloric acid (15 ml.) for 5 hr. After filtration, the solution was concentrated to a third of its volume. Ascending paper chromatography (phenol–water) of this solution, together with an authentic sample of L-glutamic acid, gave identical R_F values.

5-*Diazo*-4-*oxo*-L-*norvaline* (V). The ester (IV) (2 g.) was dissolved in 0·1N-tetraethylammonium hydroxide (200 ml.) and left for 30 min. The solution darkened, but much less than when treated with alkali hydroxide of the same concentration, as in previous experiments. The pH was then adjusted to 6·2 by addition of trifluoroacetic acid (Beckman Model G pH meter). By freeze-drying the mixture a dark brown material was obtained which was triturated with dry methanol and filtered. Recrystallisation from 75% methanol (it must be filtered hot to free it from dark impurities) gave orange needles, forming spherical aggregates which decomposed explosively at about 140° (0·235 g., 20%) (Found: C, 37·7; H, 4·8; N, 24·8; diazo-N, 18·0. $C_5H_7O_3N_3$ requires C, 38·2; H, 4·5; N, 26·8; diazo-N, 17·9%). Accurate polarimetric determinations could not be made because the substance is strongly coloured, thus allowing measurements only at very low concentrations. 5-Diazo-4-oxo-L-norvaline (V) has an infrared spectrum which is very similar to that of DON,[1] possessing strong absorption bands at 2·90, 3·20, 3·31, 3·80, 4·20, 4·70, 6·10, 2·29, 6·67, 6·90, 7·18, 7·40, 7·58, 7·70, 8·0, 8·68, and 8·81 μ. Its ultraviolet absorption spectrum also conforms to that of DON,[1] having max. at 274 mμ ($E_{1\,cm.}^{1\%}$ 600) and at 244 mμ ($E_{1\,cm.}^{1\%}$ 310).

N-*Benzyloxycarbonyl*-5-*diazo*-4-*oxo*-L-*norvaline benzyl ester*. α-Benzyl hydrogen *N*-benzyloxycarbonyl-L-aspartate [7] (2 g.) was dissolved in dry ether (30 ml.) and cooled in an ice-bath. Phosphorus pentachloride (1·25 g.) was added and the mixture shaken for 15 min. at 0° and for an additional 15 min. at room temperature. After filtration, the solvent was evaporated *in vacuo*. The residue was redissolved in dry ether and added to ethereal diazomethane (large excess). The mixture was left for a few hours, then filtered, and evaporated *in vacuo*. The residual *ester*, recrystallised from propan-1-ol, had m. p. 78—79° (0·9 g., 41%) (Found: C, 62·6; H, 5·1; N, 9·4. $C_{20}H_{19}O_5N_3$ requires C, 62·9; H, 5·0; N, 11·0%).

DEPARTMENT OF ORGANIC CHEMISTRY,
THE HEBREW UNIVERSITY, JERUSALEM, ISRAEL. [*Received, October 6th*, 1958.]

[7] Bergmann, Zervas, and Salzmann, *Ber.*, 1933, **66**, 1288.

XUM

257. *Alkaline Hydrolysis of Ethyl 1-Naphthoates. Steric Inhibition of Mesomerism involving the 4-Dimethylamino-substituent.*

By A. Fischer, Helen M. Fountain, and J. Vaughan.

Rates of alkaline hydrolysis, in 85% (w/w) ethanol–water, of several substituted ethyl 1-naphthoates have previously been communicated.[1,2] For 3- and 4-substituents an excellent fit to the Hammett equation was obtained, except with the 4-nitro-group. It was suggested that deviation for this substituent is the result of steric inhibition of mesomerism; the *peri*-hydrogen atom (at position 5) prevents coplanarity of the nitro-group and the naphthalene ring. We have now measured similar rate constants for ethyl 4-fluoro-, 4-methoxy-, and 4-dimethylamino-1-naphthoate at 50°: these substituents sometimes show deviations from a Hammett plot. The dimethylamino-substituent in particular was expected to show a deviation more marked than that of the 4-nitro-group, because the resonance component of the Hammett substituent constant (σ) is greater for the amino- than for the nitro-group. Thus Taft [3] has estimated for p-NO_2 a resonance component (σ_R) of +0·15 and an inductive component (σ_I) of +0·64. For p-NH_2, σ_R is −0·76 and σ_I +0·1: the M-effect is proportionately much greater for the amino-group and a similar conclusion should hold when the amino-group is methylated.

Experimental.—Esters. These were prepared from the acids by the Fischer–Speier method. Physical constants and relevant analyses were as follows: *ethyl 4-fluoro-*, b. p. 123°/2·5 mm. (Found: C, 71·6; H, 4·8; F, 8·3. $C_{11}H_7O_2F$ requires C, 71·6; H, 5·0; F, 8·7%), *4-methoxy-*, m. p. 65·5° (Found: C, 73·1; H, 6·0. $C_{14}H_{14}O_3$ requires C, 73·1; H, 6·1%), and *4-dimethylamino-1-naphthoate*, b. p. 152°/1 mm. (Found: N, 5·9. $C_{15}H_{17}O_2N$ requires N, 5·8%). 4-Dimethylamino-1-naphthoic acid, m. 161°, was obtained in 20% yield from 4-bromo-*NN*-dimethyl-1-naphthylamine by carboxylation of the lithium compound formed by refluxing the amine (0·04 mole) and butyl-lithium (0·054 mole) in ether (50 ml.) for 13 hr.

Hydrolyses. The method for following kinetics, using stainless steel reaction vessels, has been described.[2] Kinetic results are given in Table 1. The good agreement between the mean value found for ethyl 1-naphthoate ($k_{50} = 2{\cdot}50 \times 10^{-3}$ l. mole^{-1} sec.$^{-1}$) and the earlier reported figure ($2{\cdot}42 \times 10^{-3}$) indicates that the tabulated rate constants for substituted esters should be fully comparable with results of previous studies. It is estimated that mean k values are accurate to 5%.

Table 1. *Ethyl X-1-naphthoates in* 85% *w/w ethanol.*

X	Rate constant $10^{-3}k_{50}$	Mean 10^3k_{50}
H	2·50, 2·48, 2·39, 2·51, 2·61	2·50
4-F	4·86, 4·59, 4·66, 4·58, 4·44	4·63
4-OMe	0·636, 0·612, 0·640, 0·625, 0·639, 0·645	0·633
4-NMe_2	0·747, 0·764, 0·791, 0·764	0·766

Discussion.—A regression line has been fitted to the log k_{50} *versus* σ data for ethyl 1-naphthoate containing the following substituents: H, 3-Cl, 4-Cl, 3-Br, 4-Br, 3-Me, 4-Me, 4-F, 4-OMe. The substituent constants used are those listed by McDaniel and Brown.[4] For hydrolysis of ethyl X-1-naphthoates the slope (ρ) of the best Hammett regression line is 2·21, the calculated log k_0 is −2·585, and the correlation coefficient is 0·997. From the expression $\sigma_n = (\log k_{50} + 2{\cdot}585)/2{\cdot}21$, substituent constant values (σ_n, see ref. 2) applicable to this reaction have been calculated and are given, together with McDaniel and Brown's values (σ), in Table 2. This shows that the largest deviations occur with the 4-F, the 4-NO_2 and, outstandingly, the 4-NMe_2 substituent. No steric inhibition of mesomerism is observed for the methoxy-group, presumably because it can lie in the plane of the naphthalene ring with its methyl group "*trans*" to the *peri*-hydrogen atom. On the other hand, for the substituted amino-group, as for the nitro-substituent, inhibition of mesomerism is to be expected. Of these two groups, the very much greater deviation, from the normal σ value, of the dimethylamino-group is in accord with prediction. Resonance

[1] Fischer, Murdoch, Packer, Topsom, and Vaughan, *J.*, 1957, 4358.
[2] Fischer, Mitchell, Ogilvie, Packer, Packer, and Vaughan, *J.*, 1958, 1426.
[3] Taft, *J. Amer. Chem. Soc.*, 1957, **79**, 1045.
[4] McDaniel and Brown, *J. Org. Chem.*, 1958, **23**, 420.

TABLE 2.

Subst.	H	3-NO_2	3-Cl	4-Cl	3-Br	4-Br
σ_n	−0·013	0·703	0·368	0·242	0·368	0·255
σ	0·000	0·710	0·373	0·227	0·391	0·232
Deviation	−0·013	−0·007	−0·007	+0·015	−0·023	−0·023
Subst.	3-Me	4-Me	4-F	4-OMe	4-NO_2	4-NMe_2
σ_n	−0·075	−0·165	0·115	−0·278	0·721	−0·24
σ	−0·069	−0·170	0·062	−0·268	0·778	−0·83
Deviation	−0·006	+0·005	+0·053	−0·010	−0·057	+0·59

inhibition of this substituent has been observed previously in the alkaline hydrolysis of benzoate esters carrying one [5] or two [6] methyl groups adjacent to it: for one methyl group the substituent constant for the dimethylamino-group is −0·36. Thus the steric inhibition of mesomerism resulting from a single *ortho*-methyl group is quite marked. It has been shown recently [7] that a *peri*-CH group of naphthalene has a slightly greater steric effect than an *ortho*-methyl substituent of a benzene derivative, since the strain in 1-methylnaphthalene is measurably greater than that in *o*-xylene. For comparison with this result, values of substituent constants derived from ester hydrolysis indicate that the *peri*-CH grouping has a steric effect at least equal to that of an *ortho*-methyl group.

We thank Dr. A. D. Campbell, University of Otago, for the microanalyses and the Research Committee of the University of New Zealand for a grant.

UNIVERSITY OF CANTERBURY,
CHRISTCHURCH, NEW ZEALAND. [*Received, October 6th*, 1958.]

[5] Price and Lincoln, *J. Amer. Chem. Soc.*, 1951, **73**, 5838.
[6] Westheimer and Metcalf, *ibid.*, 1941, **63**, 1339.
[7] Packer, Vaughan, and Wong, *ibid.*, 1958, **80**, 905.

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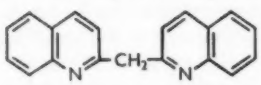
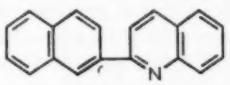
258. *ω-Halogenomethyl-pyridines, -quinolines, and -isoquinolines. Part VIII.* The Formation of 2-β-Naphthylquinoline from Di-2-quinolylmethane.*

By B. R. BROWN, D. LL. HAMMICK, J. NEWBOULD, and A. L. PRICE.

IN the preparation of di-2-quinolylmethane (I) from 2-chloro- or 2-bromo-quinoline and quinaldine, difficulty was experienced in repeating the work of Scheibe and Schmidt.[1,2] When vigorous conditions were used, chromatography of the products on alumina showed that, as well as diquinolylmethane, a small amount of another compound, m. p. 163°, was produced which by comparison with a synthetic specimen was identified as 2-β-naphthylquinoline (II).

(I)  (II) 

We have proved that 2-β-naphthylquinoline results from the reaction of diquinolylmethane with quinaldine hydrobromide in quinaldine at the boiling point. Presumably it is formed by this route during the preparation of diquinolylmethane. Careful purification of the starting materials has shown that in neither preparation does the naphthylquinoline arise from impurities, but at this stage it is not profitable to speculate on the mechanism of this remarkable change in which the nitrogen atom of a quinoline ring is eliminated.

Experimental.—2-β-Naphthylquinoline [3] separated from ethanol as pale yellow plates, m. p. 163° (Found: C, 89·2; H, 5·1; N, 5·5. Calc. for $C_{19}H_{13}N$: C, 89·45; H, 5·1; N, 5·5%). The *picrate* separated from ethanol as yellow plates, m. p. 174° (Found: C, 61·4; H, 3·85; N, 10·5. $C_{25}H_{16}O_7N_4,C_2H_6O$ requires C, 61·1; H, 4·15; N, 10·6%).

Reaction of 2-bromoquinoline with quinaldine. A mixture of 2-bromoquinoline (7·2 g.) and

* Part VII, *J.*, 1957, 5073.

[1] Scheibe, *Ber.*, 1921, **54**, 786.
[2] Scheibe and Schmidt, *Ber.*, 1922, **55**, 3159.
[3] Buu-Hoï and Cagniant, *Rec. Trav. chim.*, 1943, **62**, 713.

quinaldine (15 ml.) was heated to boiling during 20 min. and refluxed gently for 20 min. After extraction with acetone (400 ml.) and steam-distillation, the residual aqueous mixture was extracted with benzene (800 ml.), and the extract concentrated to 50 ml., and chromatographed on alumina (Spence Grade O; 300 g.). Elution with benzene (1 l.) yielded 2-β-naphthylquinoline (20 mg.) which separated from ethanol as pale yellow plates, m. p. and mixed m. p. 163° (Found: C, 89·1, 89·2; H, 5·45, 5·2; N, 5·4, 5·0%). The infrared and ultraviolet spectra were identical with those of an authentic specimen. The picrate separated from ethanol as yellow plates, m. p. and mixed m. p. 174° (Found: C, 61·0; H, 4·1; N, 10·9%).

Further elution with benzene–ether (1 : 1 v/v; 3 l.) yielded di-2-quinolylmethane (1·4 g.) which separated from light petroleum (b. p. 100—120°) as pink needles, m. p. 102°.

A similar experiment with 2-chloroquinoline gave the same products.

Reaction of di-2-quinolylmethane with quinaldine hydrobromide. Diquinolylmethane (3·3 g.), quinaldine (3·8 ml.), and quinaldine hydrobromide (1·25 g.) were brought to boiling during 30 min. and refluxed for 40 min. Extraction and chromatography as above yielded a yellow oil (0·30 g.) and unchanged diquinolylmethane (2·0 g.). Chromatography of the yellow oil yielded 2-β-naphthylquinoline which separated from ethanol as pale yellow plates (3 mg.), m. p. and mixed m. p. 162°. The infrared spectrum was identical with that of the synthetic specimen.

DYSON PERRINS LABORATORY, OXFORD UNIVERSITY. [*Received, October 29th*, 1958.]

259. *Studies of the Coal-tar Bases. Part VIII.* Isolation of 2 : 3 : 6-Trimethylpyridine from the Collidine Fraction.*

By R. F. EVANS.

PREVIOUS Parts described the successful application of fractional distillation to the separation of constituents of the picoline [1,2] and lutidine [3] fractions of coal-tar bases. Fractional distillation of the collidine fraction, either alone or mixed with an azeotrope-forming substance such as phenol,[3] removes minor constituents such as 3-ethylpyridine, but does not bring about worthwhile separation of the two major components, 2 : 3 : 6- and 2 : 4 : 6-trimethylpyridine. This is in accord with the results of earlier investigators [4-7] who combined fractional distillation and fractional precipitation with picric or picrolonic acids to obtain small quantities of purified 2 : 3 : 6-trimethylpyridine from a mixture of coal-tar or petroleum bases. This being laborious, Tsuda *et al.*[8] synthesised 2 : 3 : 6-trimethylpyridine for use in dissociation constant experiments [9] in preference to using a specimen from coal-tar.

Since we were interested in the isolation of 2 : 3 : 6-trimethylpyridine in kilogram quantities, a promising new chemical approach was initiated. A binary mixture of 2 : 3 : 6- and 2 : 4 : 6-trimethylpyridine, produced by precise fractional distillation under reduced pressure of a crude collidine fraction, was converted into the *N*-oxides which were then treated with concentrated nitric and sulphuric acids. 2 : 3 : 6-Trimethylpyridine *N*-oxide, the only pyridine *N*-oxide present with a vacant 4-position, was the only constituent nitrated. 2 : 3 : 6-Trimethyl-4-nitropyridine *N*-oxide, a high-melting solid, separated easily and was easily purified. The nitro-group could be replaced by chlorine by heating with concentrated hydrochloric acid; the temperature (190°) required for this nucleophilic replacement was much higher than that (110°) required for the corresponding transformation in 4-nitropyridine *N*-oxide,[10] and reflected the adverse effect of three methyl groups releasing electrons to the pyridine nucleus. A two-stage reduction of 4-chloro-2 : 3 : 6-trimethylpyridine *N*-oxide afforded pure 2 : 3 : 6-trimethylpyridine.

* Part VII, Coulson and Ditcham, *J.*, 1957, 356.

[1] Coulson and Jones, *J. Soc. Chem. Ind.*, 1946, **65**, 169.
[2] Jones, *ibid.*, 1950, **69**, 99.
[3] Coulson, Hales, Holt, and Ditcham, *J. Appl. Chem.*, 1952, **2**, 71.
[4] Eckert and Loria, *Monatsh.*, 1917, **38**, 225.
[5] Hackmann, Wibaut, and Gitsels, *Rec. Trav. chim.*, 1943, **62**, 229.
[6] Matsumoto and Ihara, *Coal Tar (J. Japan Tar Ind. Assoc.)*, 1951, **3**, 224; *Chem. Abs.*, 1952, **46**, 7741.
[7] Fushizaki, *Technol. Repts. Osaka Univ.*, 1951, **1**, 309; *Chem. Abs.*, 1592, **46**, 7746.
[8] Tsuda, Ikekawa, Iino, Furukawa, and Hattori, *Pharm. Bull. (Japan)*, 1953, **1**, 126.
[9] Ikekawa, Sato, and Maeda, *ibid.*, 1954, **2**, 205.
[10] Den Hertog and Combé, *Rec. Trav. chim.*, 1951, **70**, 581.

Experimental.—Microanalyses and infrared spectral measurements were carried out by Miss M. Corner and Mr. W. Kynaston respectively of this laboratory. M. p.s are corrected.

Oxidation of collidines. The starting material was a fraction, b. p. 107—108°/100 mm., which was obtained by the refractionation through a 50-plate column of a crude collidine fraction kindly supplied by Messrs. Yorkshire Tar Distillers Ltd. Infrared analysis revealed that this fraction was a binary mixture of 2 : 3 : 6-trimethylpyridine (*ca.* 65% w/w) and its 2 : 4 : 6-isomer.

This binary mixture (121 g.) was quantitatively converted into the *N*-oxides with glacial acetic acid (600 ml.) and hydrogen peroxide (198 ml., 30%) according to Ochiai's procedure.[11]

2 : 3 : 6-*Trimethyl*-4-*nitropyridine N-oxide.* The mixed *N*-oxides (68·5 g., 0·5 mole), concentrated sulphuric acid (200 ml., *d* 1·98) and concentrated nitric acid (50 ml., *d* 1·42) were heated on the steam-bath under reflux for 7½ hr. The cold mixture was poured into 2 l. of water and the solution was made slightly alkaline with sodium hydroxide solution. After cooling, the solid yellow nitro-compound (21 g.) was filtered off. Chloroform extraction of the filtrate led to the recovery of additional nitro-compound (3·5 g.) giving a total yield of 40% based on the amount of 2 : 3 : 6-trimethylpyridine present in the starting material. After two crystallisations from alcohol, 2 : 3 : 6-*trimethyl*-4-*nitropyridine* N-*oxide* had m. p. 115·5—117° [Found: C, 52·7; H, 5·7; N, 15·2. $C_8H_{10}O_3N_2$ requires C, 52·7; H, 5·5; N, 15·4%].

4-*Chloro*-2 : 3 : 6-*trimethylpyridine* N-*oxide.* Nitro-compound (20·2 g.) and hydrochloric acid (95 ml. of 24%) were heated at 190—200° in a sealed tube for 24 hr. The mixture was evaporated at 100°/20 mm., the residue was dissolved in water and titrated with aqueous sodium hydroxide to a phenolphthalein end-point. The solution was again evaporated to dryness at 100°/20 mm. and the solid residue was extracted four times with boiling alcohol. Evaporation of the alcoholic extract furnished 4-*chloro*-2 : 3 : 6-*trimethylpyridine* N-*oxide* (16 g., 92%) which crystallised from acetone in white needles, m. p. 135—137·5° [Found: C, 56·2; H, 6·2; N, 7·9; Cl, 20·7. $C_8H_{10}ONCl$ requires C, 56·0; H, 5·9; N, 8·2; Cl, 20·7%].

4-*Chloro*-2 : 3 : 6-*trimethylpyridine*. 4-Chloro-2 : 3 : 6-trimethylpyridine *N*-oxide (7·25 g.), iron powder (4 g.), and glacial acetic acid (40 ml.) were heated on the steam-bath under reflux for 2 hr. The mixture was made alkaline with aqueous sodium hydroxide and steam-distilled for 2 hr. The aqueous distillate being cooled in ice, 4-*chloro*-2 : 3 : 6-*trimethylpyridine* (6·0 g.), m. p. 33·5—34·5°, separated (Found: C, 61·8; H, 6·5; N, 8·6. $C_8H_{10}ONCl$ requires C, 61·8; H, 6·5; N, 9·0%). Ether-extraction of the filtrate gave additional material (0·9 g.) which brought the total yield of chloro-compound almost to 100%. The *picrate* crystallised in yellow needles, m. p. 139·5—141·5°, from alcohol [Found: C, 43·6; H, 3·5; N, 14·6. $C_{14}H_{13}O_7N_4Cl$ requires C, 43·7; H, 3·4; N, 14·6%].

2 : 3 : 6-*Trimethylpyridine.* In a typical experiment, 4-chloro-2 : 3 : 6-trimethylpyridine (6·6 g.), potassium acetate (5 g.), methanol (25 ml.), and palladium chloride (1 g.) were shaken with hydrogen at room temperature and atmospheric pressure until no more hydrogen was absorbed (4½ hr.). The mixture was filtered and the filtrate evaporated on the steam-bath. Water was added to the residue, which was made alkaline with aqueous sodium hydroxide and twice extracted with ether. The ether extract was dried (Na_2SO_4) and distilled to give 2 : 3 : 6-trimethylpyridine (2·5 g., 49%), b. p. 172°. The infrared spectrum of this material revealed the absence of 2 : 4 : 6-trimethylpyridine. The picrate crystallised as yellow needles, m. p. 146—148° (lit., m. p. 144·5—145·5°,[8] 148—149° [5]), from alcohol (Found: C, 48·45; H, 4·4; N, 15·3. Calc. for $C_{14}H_{14}O_7N_4$: C, 48·0; H, 4·0; N, 15·9%).

National Chemical Laboratory, D.S.I.R., Teddington. [*Received, November 10th,* 1958.]

[11] Ochiai, *J. Org. Chem.*, 1953, **18**, 534.

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260. *Hydrolysis of "Ethyl Methylenecitrate" [5 : 5-Di(ethoxycarbonylmethyl)-1 : 3-dioxolan-4-one], and an Attempted Synthesis of Agaric Acid.*

By D. W. S. Evans.

One optical form of agaric acid (α-hexadecylcitric acid) occurs in the Basidiomycete, *Polyporus officinalis*, Vill. In an attempt to synthesise this acid two preliminary investigations were undertaken. First, it was confirmed that an ester containing an α-CH_2 group could be monoalkylated by the Hudson and Hauser technique,[1] although

[1] Hudson and Hauser, *J. Amer. Chem. Soc.*, 1940, **62**, 2457; 1941, **63**, 3156.

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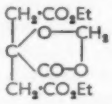
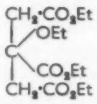
the yield was poor (13·2% for ethyl α-methylbutyrate). Secondly, it was found as the result of a large number of experiments, in which conditions (nature and amount of hydrolysing agent, duration of reaction, and temperature) were varied widely, that compound (I) could be converted in high yield (about 80%) into citric acid by hydrolysis with cold aqueous sodium hydroxide followed by aqueous ammonia under pressure to effect ring opening. An alternative method (catalytic hydrogenation) did not open the methylene ring. [Several attempts to regenerate citric acid from "methylenecitric acid" or its ester (I) have been reported.[2-4]]

(I)   (II)

When the ester (I) was converted into its α-hexadecyl derivative by Hudson and Hauser's method [1] and the product hydrolysed, the only significant substance isolated was a small amount of stearic acid: von Thoms and Vogelsang [5] showed that stearic acid is a product of alkaline decomposition of agaric acid. The instability of the latter is well known,[6] and it appears that in the attempted synthesis the conditions necessary for removal of the protecting ring structure were too rigorous to allow the survival of the desired product. An attempt to prepare agaric acid by monoalkylation of the ethyl ether (II) was also abortive.

Experimental.—"*Ethyl methylenecitrate*" [5 : 5-*di*(*ethoxycarbonylmethyl*)-1 : 3-*dioxolan*-4-*one*] (I). This was obtained by the following modification of the method of Bayer & Co.[4] "Methylenecitric acid" [3] (131 g.) was heated for 5 hr. under reflux with absolute alcohol (505 ml.), and sulphuric acid (17·2 ml.), then cooled and poured into ice-cold water (1 l.). The crystals were separated, washed three times by stirring with cold water, collected, and dried. They melted at 47°, and did not lose weight on storage as a powder for three days *in vacuo* over phosphoric anhydride. However, when the ester was dissolved in benzene, water equivalent to about 30% of the weight of ester separated. The water was run off, more benzene added, and the solution dried in a Dean and Starke apparatus. After removal of excess of solvent it deposited the ester (65 g., 39%), m. p. 54°, unchanged on further crystallisation from benzene (Bayer & Co.[4] gave m. p. 55°) (Found: C, 50·9; H, 6·4. Calc. for $C_{11}H_{16}O_7$: C, 50·8; H, 6·2%).

Optimum conversion into citric acid. The ester (I) (5 g.) was shaken vigorously for 90 hr. at room temperature with 2N-sodium hydroxide (25 ml.). 2N-Ammonia (38 ml.) was added to the faintly yellow solution, and the mixture was transferred to five 30 ml. soft-glass tubes with well-collapsed bottom seals. These were closed and kept at 100° for 20 hr., the usual precautions being taken. The combined dark orange liquors were acidified (with 6N-hydrochloric acid, 14 ml.), mostly decolorised with carbon, and diluted to 1500 ml. A 10 ml. aliquot part then contained 24·6 mg. (78·3%) of citric acid (assayed absorptiometrically [7]). The remainder was concentrated and again treated with carbon, and the acid obtained through its barium salt as colourless hygroscopic crystals of m. p. 153° (after drying at 120°) [Found: equiv., 63·9. Calc. for $C_3H_5O(CO_2H)_3$: equiv., 64·0]. Its *p*-bromophenacyl ester had m. p. and mixed m. p. 146·8° (three crystallisations from 65% ethanol). The *p*-nitrobenzyl ester after one similar recrystallisation had m. p. and mixed m. p. 103°.

I thank the Ministry of Education for a grant.

THE UNIVERSITY, NOTTINGHAM. [*Received, November 17th*, 1958.]

[2] de Bruyn and van Ekenstein, *Rec. Trav. chim.*, 1901, **20**, 231; Chem. Farb. Schering., Friedlander's "Fortschritte," 1901, Vol. VI, p. 1222.
[3] Sternberg, *Pharm. Ztg.*, 1901, **46**, 1004.
[4] Bayer & Co., Friedlander's "Fortschritte," 1908, Vol. IX, p. 899 (see, however, Hanzlik, *J. Urol.*, 1920, **4**, 145).
[5] von Thoms and Vogelsang, *Annalen*, 1907, **357**, 145.
[6] Schmieder, *Arch. Pharm.*, 1886, **224**, 661.
[7] Hunter and Leloir, *J. Biol. Chem.*, 1945, **159**, 295.

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